STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 168937

TO: Sarvamangala Devi **Art Unit:** 1645 **Location:** REM-3C18 **Serial Number:** ~~09/393590~~ **Friday, October 28, 2005**	**From:** Beverly Shears **Location:** Biotech-Chem Library REM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

Search Notes

168937

STIC-Biotech/ChemLib

From: Devi, Sarvamangala
Sent: Wednesday, October 19, 2005 8:42 AM
To: STIC-Biotech/ChemLib
Cc: Shears, Beverly
Subject: 09393590

Please ask **Ms. BEVERLY SHEARS** to perform this search.

Please perform a text search and an inventors' name search in application 09/393,590. Inventors: Elizabeth Moyer and Pamela Hirtzer.

Claim 1. A stable stabilized liquid pharmaceutical botulinum toxin (BOTOX) formulation for therapeutic use in humans, comprising a pharmaceutically acceptable buffered saline capable of providing a buffered pH range to the formulation between pH 5 and pH 6 and
a therapeutic concentration suitable for use in humans of purified botulinum toxin; and the formulation is capable of being stable as a liquid when stored for at least one year at a temperature between 0 and 10 degrees centigrade ± 10%.
Claim 2. The formulation of claim 1, wherein said temperature is 5 ± 3 degrees centigrade.
Claim 3. The formulation of claim 1, wherein said temperature is 4 ± 2 degrees centigrade.
Claim 4. The formulation of claim 1, wherein said buffered pH is pH 5.6.
Claim 5. The formulation of claim 1, wherein said toxin formulation is stable in liquid form for at least two years.
Claim 6. The formulation of claim 1, wherein said buffered saline has a pK in the range of pH 4.5-6.5.
Claim 7. The formulation of claim 6, wherein said buffered saline is phosphate buffer, phosphate-citrate buffer, acetate buffer, and succinate buffer.
Claim 8. The formulation of claim 1, wherein said botulinum toxin is of a botulinum toxin type A, B, C1, C2, D, E, F or G.
Claim 9. The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type B present at a concentration in the range of 10 U-20,000 U/ml ± 10%.
Claim 10. The formulation of claim 9, wherein said botulinum toxin Type B is present in a high molecular weight complex of 700 ± 10% kilodaltons.
Claim 11. The formulation of claim 9, wherein said botulinum toxin Type B is present at a concentration between 1000-5000 U/ml.
Claim 12. The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of between 20-2000 U/m1.
Claim 13. The formulation of claim 12, wherein said botulinum toxin Type A is present at a concentration in the range of between 100-1000 U/m1.
Claim 14. The formulation of claim 1, which further includes an excipient protein selected from the group consisting of serum albumin, recombinant human serum albumin, and gelatin.
Claim 16. A stabilized liquid pharmaceutical botulinum toxin formulation for therapeutic use in humans, comprising a pharmaceutically acceptable liquid buffered saline capable of providing a buffered pH range to the formulation between pH 5 and pH 6 and
a therapeutic concentration suitable for use in humans of purified botulinum toxin; and the toxin formulation is capable of being stable as a liquid when stored for at least about 6 months at a temperature between 10 and 30 ± 10% degrees centigrade.
Claim 17. The formulation of claim 16, wherein said temperature is 25 degree centigrade.
Claim 18. The formulation of claim 16, wherein said buffered pH range is pH 5.6.
Claim 19. The fonuulation of claim 16, wherein said buffered saline has a pK in the range of pH 4.5-6.5.
Claim 20. The formulation of claim 19, wherein said buffered saline is phosphate buffer, phosphate-citrate buffer, or succinate buffer.
Claim 21. The formulation of claim 16, wherein said botulinum toxin is of botulinum toxin type A, B, Cl, C2, D, E, F or G.
Claim 22. The fonnulation of claim 21, wherein said botulinum toxin is botulinum toxin Type B present at a concentration of between 100-20,000 U/ml ± 10%.

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Searcher:_____
Searcher Phone:_____
Date Searcher Picked up:_____
Date completed:_____
Searcher Prep Time:_____
Online Time:_____

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Type of Search
NA#_____ AA#:_____
S/L:_____ Oligomer:_____
Encode/Transl:_____
Structure #:_____Text:_____
Inventor:_____ Litigation:_____

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Vendors and cost where applicable
STN:_____
DIALOG:_____
QUESTEL/ORBIT:_____
LEXIS/NEXIS:_____
SEQUENCE SYSTEM:_____
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Date completed: _____
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Number of Searches: _____
Number of Databases: _____

Search Site
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Type of Search
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Vendors
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✓ STN
✓ Dialog
_____ APS
_____ Geninfo
_____ SDC
_____ DARC/Questel
_____ Other

(9-90)

Devi, S.
09139 3590

FILE 'REGISTRY' ENTERED AT 11:52:32 ON 27 OCT 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 OCT 2005 HIGHEST RN 866186-08-5
DICTIONARY FILE UPDATES: 26 OCT 2005 HIGHEST RN 866186-08-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

- key terms

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                E BOTOX/CN 5
L1            1 SEA ABB=ON  PLU=ON  BOTOX/CN
                E BOTULIN TOXIN/CN 5
L2            6 SEA ABB=ON  PLU=ON  BOTULIN TOXIN? /CN
L3            8 SEA ABB=ON  PLU=ON  BOTULIN NEUROTOXIN? /CN
L4            8 SEA ABB=ON  PLU=ON  BOTULINUM TOXIN? /CN
L5           14 SEA ABB=ON  PLU=ON  BOTULINUM NEUROTOXIN? /CN
L6          134 SEA ABB=ON  PLU=ON  (BOTULIN A ? OR BOTULIN B ? OR BOTULIN
                C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR BOTULIN E ? OR
                BOTULIN F ?)/CN
L7            2 SEA ABB=ON  PLU=ON  (BOTULINUM A ? OR BOTULINUM B ? OR
                BOTULINUM C1 ? OR BOTULINUM C2 ? OR BOTULINUM D ? OR
                BOTULINUM E ? OR BOTULINUM F ?)/CN
L8          156 SEA ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7

                E PHOSPHATE/CN
L9            9 SEA ABB=ON  PLU=ON  (PHOSPHATE/CN OR "PHOSPHATE (32PO4)"/CN
                 OR "PHOSPHATE (H2PO4-)"/CN OR "PHOSPHATE (H2PO41-)"/CN OR
                "PHOSPHATE (HPO42-)"/CN OR "PHOSPHATE (P2O74-)"/CN OR
                "PHOSPHATE (P4O123-)"/CN) OR "PHOSPHATE (P6O186-)"/CN OR
                ("PHOSPHATE (PO3-)"/CN OR "PHOSPHATE (PO31-)"/CN OR
                "PHOSPHATE (PO32-)"/CN) OR "PHOSPHATE (PO43-)"/CN OR
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                "PHOSPHATE (PO4H2-)"/CN
                E CITRATE/CN 5
L10           1 SEA ABB=ON  PLU=ON  CITRATE/CN
                E ACETATE/CN 5
L11           1 SEA ABB=ON  PLU=ON  ACETATE/CN
                E SUCCINATE/CN 5
L12           1 SEA ABB=ON  PLU=ON  SUCCINATE/CN
L13          12 SEA ABB=ON  PLU=ON  L9 OR L10 OR L11 OR L12
L14         445 SEA ABB=ON  PLU=ON  SODIUM CHLORIDE ?/CN

                E BONT/CN 5

L15           6 S (BOTULIN G ? OR BOTULINUM G ?)/CN
L16         161 S L8 OR L15


                E HUMAN SERUM ALBUMIN/CN 5
L21           3 S HUMAN SERUM ALBUMIN ?/CN
                E SERUM ALBUMIN/CN 5
L22          62 S SERUM ALBUMIN ?/CN
                E GELATINS/CN 5
L23           1 S E3
L24          66 S L21 OR L22 OR L23

FILE 'HCAPLUS' ENTERED AT 11:52:32 ON 27 OCT 2005
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FILE COVERS 1907 - 27 Oct 2005  VOL 143 ISS 18
FILE LAST UPDATED: 26 Oct 2005  (20051026/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTOX/CN
L2            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULIN TOXIN? /CN
L3            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULIN NEUROTOXIN? /CN
L4            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULINUM TOXIN? /CN
L5           14 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULINUM NEUROTOXIN?
                /CN
L6          134 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN A ? OR BOTULIN
                B ? OR BOTULIN C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR
                BOTULIN E ? OR BOTULIN F ?)/CN
L7            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULINUM A ? OR
                BOTULINUM B ? OR BOTULINUM C1 ? OR BOTULINUM C2 ? OR
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                BOTULINUM D ? OR BOTULINUM E ? OR BOTULINUM F ?)/CN
L8          156 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR
                L5 OR L6 OR L7
L9            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (PHOSPHATE/CN OR
                "PHOSPHATE (32PO4)"/CN OR "PHOSPHATE (H2PO4-)"/CN OR
                "PHOSPHATE (H2PO41-)"/CN OR "PHOSPHATE (HPO42-)"/CN OR
                "PHOSPHATE (P2O74-)"/CN OR "PHOSPHATE (P4O123-)"/CN) OR
                "PHOSPHATE (P6O186-)"/CN OR ("PHOSPHATE (PO3-)"/CN OR
                "PHOSPHATE (PO31-)"/CN OR "PHOSPHATE (PO32-)"/CN) OR
                "PHOSPHATE (PO43-)"/CN OR "PHOSPHATE (PO4H2-)"/CN
L10           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CITRATE/CN
L11           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACETATE/CN
L12           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SUCCINATE/CN
L13          12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 OR L10 OR L11 OR L12
L15           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN G ? OR BOTULINUM
                 G ?)/CN
L16         161 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L15
L17        4721 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR (BO OR BOTULIN?)(5A
                )(NT OR TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR
                BOTX# OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(3A)(A
                OR B OR C1 OR C2 OR D OR E OR F OR G)
L18     1354347 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR PHOSPHATE OR
                CITRATE OR ACETATE OR SUCCINATE OR SUCCINIC OR BUTANEDIOIC
                OR ACETIC
L19         246 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L18
L20          63 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND (14) OR NACL OR
                (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALINE)
L21           3 SEA FILE=REGISTRY ABB=ON  PLU=ON  HUMAN SERUM ALBUMIN ?/CN

L22          62 SEA FILE=REGISTRY ABB=ON  PLU=ON  SERUM ALBUMIN ?/CN
L23           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  GELATINS/CN
L24          66 SEA FILE=REGISTRY ABB=ON  PLU=ON  L21 OR L22 OR L23
L26           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND (L24 OR HSA OR
                ALBUMIN OR GELATIN)
```

Should read "L14". See L58 - L65

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L26  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2005 ACS on STN
ED   Entered STN:  08 Jul 2005
ACCESSION NUMBER:         2005:589208  HCAPLUS
DOCUMENT NUMBER:          143:93565
TITLE:                    Marker proteins and methods for diagnosing
                          endometrial cancer or phase
INVENTOR(S):              Colgan, Terence J.; Siu, K. W. Michael; Romaschin,
                          Alexander D.; Yang, Eric C. C.
PATENT ASSIGNEE(S):       Mount Sinai Hospital, Can.; York University;
                          University Health Network
SOURCE:                   PCT Int. Appl., 199 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005061725         A1    20050707    WO 2004-CA2172          20041221
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
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MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-532601P P 20031223
US 2004-630990P P 20041124

AB Methods for detecting endometrial diseases or an endometrium phase in a subject are described comprising measuring endometrial markers or polynucleotides encoding the markers in a sample from the subject. The invention also provides localization or imaging methods for endometrial diseases, and kits for carrying out the methods of the invention. The invention also contemplates therapeutic applications for endometrial diseases employing endometrial markers, polynucleotides encoding the markers, and/or binding agents for the markers. Thus, isotope-coded affinity tag (ICAT) anal. was used to identify differentially expressed proteins in proliferative and secretory endometria as well as in normal and cancerous endometrial tissues.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 20 Jun 2005
ACCESSION NUMBER: 2005:531598 HCAPLUS
DOCUMENT NUMBER: 143:126710
TITLE: Pilot study of the safety and efficacy of Myobloc (**botulinum toxin** type **B**) for treatment of axillary hyperhidrosis
AUTHOR(S): Baumann, Leslie; Slezinger, Anele; Halem, Monica; Vujevich, Justin; Martin, Lucy K.; Black, Laura; Bryde, Joy
CORPORATE SOURCE: Department of Dermatology and Cutaneous Surgery, Division of Cosmetic Dermatology, University of Miami School of Medicine, Miami, FL, USA
SOURCE: International Journal of Dermatology (2005), 44(5), 418-424
CODEN: IJDEBB; ISSN: 0011-9059
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: **Botulinum toxin** type **B** (BTX-B, Myobloc, San Francisco, CA, USA) was FDA-approved for the treatment of cervical dystonia in Dec. 2000. It has since been used off-label for the treatment of axillary hyperhidrosis. However, there are sparse data in the medical literature evaluating the safety and efficacy of Myobloc (**botulinum toxin** type **B**) for this indication. Objective: To assess the safety, efficacy and duration of action of Myobloc (**botulinum toxin** type **B**) in the treatment of bilateral axillary hyperhidrosis. Methods: This study was a double-blinded, randomized, pilot study conducted in an outpatient office setting at a private academic medical center beginning in Nov. 2001. Twenty-three male and

female volunteers between the ages of 18 and 80 were screened for participation; 20 participants with primary axillary hyperhidrosis were enrolled. Participants were injected s.c. with either Myobloc (**botulinum toxin** type **B**) (2500 U, or 0.5 mL, per axilla) or 0.5 mL vehicle (100 mM **NaCl**, 10 mM **succinate**, and 0.5 mg/mL human **albumin**) into bilateral axillae. Participants who received placebo were rolled over and received Myobloc (**botulinum toxin** type **B**) at subsequent visits. All participants were followed until sweating returned to baseline levels. This trial was initially conceived as a placebo-controlled study; however, owing to the insufficient size of the placebo group, the placebo arm of this trial was dropped during data anal. The main outcome measures were safety, efficacy, and duration of effect. Results: According to participant assessment of axillary hyperhidrosis improvement (A-HI) and quality of life (A-HQOL) scores and the physician assessment scores, a significant difference was observed in treatment response at Day 30 in the participants receiving Myobloc (**botulinum toxin** type **B**) injections. Duration of action ranged from 2.2 to 8.1 mo (mean 5.0 mo). The adverse event profile included bruising, flu-like symptoms, and dry eyes. Conclusion: Myobloc (**botulinum toxin** type **B**) proved to be safe and efficacious for the treatment of bilateral axillary hyperhidrosis. More studies are needed to assess the duration of response using different doses of Myobloc (**botulinum toxin** type **B**).

IT **93384-44-2**, Myobloc
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pilot study showed Myobloc was safe and effective with acceptable duration of action and minimal adverse events in treatment of patient with bilateral axillary hyperhidrosis)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Dec 2003
ACCESSION NUMBER: 2003:950462 HCAPLUS
DOCUMENT NUMBER: 140:8814
TITLE: Pharmaceutical preparation of **botulinum neurotoxin**
INVENTOR(S): Zabudkin, Alexander F.; Krasnopolsky, Juri M.; Itkin, Aleksandr M.; Itkin, Dmitry M.
PATENT ASSIGNEE(S): Ukraine
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003224020	A1	20031204	US 2003-447417	20030528
WO 2003101483	A1	20031211	WO 2003-US16869	20030528

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-385286P P 20020531

AB A pharmaceutical preparation of **botulinum neurotoxins** free of human blood products (such as human **albumin**), the preparation comprising **a botulinum neurotoxin** incorporated in phosphatidylcholine liposomes. A flask is filled with a solution of phosphatidylcholine in ethanol containing 0.1 g lipid. The solution is subjected to evaporation at 35° until a lipid film is formed. He lipid film is then resuspended in 10-L sterile 0.9% **sodium chloride** solution with 7.0-7.4 **phosphate** buffer containing 1 mg of **botulinum** type **A neurotoxin** complex (95-98% purity). After the lipid film is successfully resuspended from the flask walls, the resulting emulsion is thoroughly mixed for 30 min until homogeneous emulsion is produced. Such emulsion is then transferred into a homogenizing reactor and the emulsion is homogenized at a pressure of 60 MPa and a temperature of 30-35°. When an optical d. of 0.1-0.12 is achieved, 25 g lactose is added to the emulsion. The resulting emulsion is then sequentially filtered. The resulting sterile emulsion is then distributed into vials or ampuls, each containing 0.1 mL sterile emulsion. The vials or ampuls are deep frozen at -70° for 48 h, followed by lyophilization. After lyophilization, the vials are hermetically sealed with an atmospheric of inert gas introduced over the lyophilized emulsion in the vial.

IT **93384-43-1, Botulin A 93384-44-2, Botulin B 93384-46-4, Botulin D 93384-47-5, Botulin E 107231-12-9, Botulin 107231-13-0, Botulin C1 107231-14-1, Botulin C2 107231-15-2, Botulin F 107231-16-3, Botulin G**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical preparation of **botulinum neurotoxin**)

L26 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 24 Mar 2000
ACCESSION NUMBER: 2000:190943 HCAPLUS
DOCUMENT NUMBER: 132:227422
TITLE: Stable liquid formulations of **Botulinum toxin**
INVENTOR(S): Moyer, Elizabeth; Hirtzer, Pamela
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000015245	A2	20000323	WO 1999-US20912		19990909
WO 2000015245	A3	20000608			
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
TW 574036	B	20040201	TW 1999-88114941		19990831
CA 2342243	AA	20000323	CA 1999-2342243		19990909
AU 9958214	A1	20000403	AU 1999-58214		19990909
AU 755556	B2	20021212			
BR 9913585	A	20010605	BR 1999-13585		19990909
EP 1112082	A2	20010704	EP 1999-945649		19990909
EP 1112082	B1	20020731			
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TR 200100728	T2	20010821	TR 2001-200100728		19990909
SI 20566	C	20011231	SI 1999-20081		19990909
EE 200100140	A	20020617	EE 2001-140		19990909
JP 2002524527	T2	20020806	JP 2000-569829		19990909
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ES 2181473	T3	20030216	ES 1999-945649		19990909
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NO 2001001207	A	20010509	NO 2001-1207		20010309
LV 12684	B	20011020	LV 2001-56		20010410
BG 105435	A	20011231	BG 2001-105435		20010410
LT 4959	B	20021025	LT 2001-41		20010410
PRIORITY APPLN. INFO.:			US 1998-99870P	P	19980911
			WO 1999-US20912	W	19990909

AB The invention includes liquid formulations of **botulinum toxin** that are stable to storage in liquid form at standard refrigerator temps. for at least 1-2 yr and to storage at higher temps. for at least 6 mo. The invention also includes methods of treatment using such formulations and uses of such formulations in the manufacture of medicaments for various therapeutic and cosmetic treatments. A formulation was prepared containing **Botulinum toxin** Type **B** 500±100 LD50U/mL, di-Na **succinate** 10 mM, **NaCl** 100 mM, human **albumin** 0.5 mg/mL, and HCl for pH adjustment.

IT **126-44-3, Citrate,** biological studies
14265-44-2, Phosphate, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable liquid formulations of **Botulinum toxin**)

L26 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 10 Dec 1994
ACCESSION NUMBER: 1994:674169 HCAPLUS
DOCUMENT NUMBER: 121:274169
TITLE: Recovery of type **A botulinal toxin** following lyophilization
AUTHOR(S): Goodnough, Michael C.; Johnson, Eric A.
CORPORATE SOURCE: Food Res. Inst., Univ. Wisconsin, Madison, WI, 53706, USA

SOURCE: ACS Symposium Series (1994), 567(Formulation and Delivery of Proteins and Peptides), 193-203
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Type **A botulinum toxin** is diluted to very low concns. (ng/mL) for medical use and preserved by lyophilization in a mixture of human serum **albumin** and **sodium chloride** at a slightly alkaline pH. This com. process results in considerable loss of activity. In this study, conditions were found that gave >90% recovery of the toxicity following lyophilization of solns. containing 20-1000 mouse 50% LDs (1-50 ng of toxin complex). Full recovery of starting toxicity was obtained upon drying 0.1 mL when the pH was maintained below 7.0 and serum **albumins** or other protein excipients were used as stabilizers without **sodium chloride**. Possible mechanisms of toxin inactivation were examined and may include aggregation, deamidation, and peptide bond hydrolysis.

L26 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 13 Dec 1992
ACCESSION NUMBER: 1992:639677 HCAPLUS
DOCUMENT NUMBER: 117:239677
TITLE: Stabilization of **botulinum toxin** type **A** during lyophilization
AUTHOR(S): Goodnough, Michael C.; Johnson, Eric A.
CORPORATE SOURCE: Dep. Food Microbiol. Toxicol., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Applied and Environmental Microbiology (1992), 58(10), 3426-8
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Botulinum toxin** for medical use is diluted to very low concns. (nanograms per mL); when it is preserved by lyophilization, considerable loss of activity can occur. In the present study, conditions that gave >90% recovery of the toxicity after lyophilization of solns. containing 20 to 1000 mouse 50% LDs per mL were found. Toxicity was recovered upon drying 0.1 mL of toxin solution when the pH was maintained below 7 and bovine or human serum **albumins** were used as stabilizers. Various other substances tested with **albumin**, including glucose, sucrose, trehalose, mannitol, glycine, and cellobiose, did not increase recovery on drying.

IT **93384-43-1, Botulin A**
RL: PROC (Process)
(stabilization of, during lyophilization)

L26 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1966:107065 HCAPLUS
DOCUMENT NUMBER: 64:107065
ORIGINAL REFERENCE NO.: 64:20234b-d
TITLE: The effect of temperature on toxin formation and **toxin** stability of Clostridium **botulinumn** type **E** in different environments
AUTHOR(S): Abrahamsson, Kerstin; Gullmar, B.; Molin, N.
CORPORATE SOURCE: Swedish Inst. Food Preserv. Res., Goteborg

SOURCE: Canadian Journal of Microbiology (1966), 12(2), 385-94
CODEN: CJMIAZ; ISSN: 0008-4166
DOCUMENT TYPE: Journal
LANGUAGE: English

AB C. **botulinum** type **E** produced **toxin** at temps. between 3° and 30° in a chopped meat medium and in a fish dialyzate. The toxin was produced more rapidly in the meat medium. No toxin was found after 1 year of incubation at 1°. At 3°, slight toxin production was noticed after 120 days, when the inoculum consisted of a mixture of vegetative cells and spores. The lowest concentration of **NaCl** necessary to inhibit toxin production varied with the incubation temperature and duration of storage. The inhibiting effect of **NaCl** was more pronounced at a lower temperature Type E spores mixed in fish-meat medium heated for 110 min. at 80° or for 10 min. at 90° produced toxin during prolonged storage at 20% but not after they were heated at 90° for 20 min. Toxin (type E) proved more thermostable in meat broth and fish dialyzate than in **phosphate** buffer solution or in buffer supplemented with **gelatin**. In meat broth, the toxin was inactivated after 5 min. at 65°.

L26 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1966:5105 HCAPLUS
DOCUMENT NUMBER: 64:5105
ORIGINAL REFERENCE NO.: 64:948e-g
TITLE: Fractionation of proteins in an aqueous medium
INVENTOR(S): Polson, Alfred
PATENT ASSIGNEE(S): South African Inventions Development Corp.
SOURCE: 9 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1006258		19650929	GB	
PRIORITY APPLN. INFO.:			ZA	19620103

AB A process is described for rendering less soluble or less dispersible in an aqueous liquid a proteinaceous substance by addition of a polyethylene glycol (I) of mol. weight 1500-20,000. The process is useful for fractionating and purifying various types of protein. Human plasma was diluted with an equal volume of H2O, giving a protein concentration of 3.8% by weight Portions of this soluble (5 ml.) were added to 5-ml. proteins of I (mol. weight 6000) (II) of increasing concentration dissolved in a 1/3M **phosphate** buffer of pH 7.0. The mixts. were kept at 21° for 30 min. then spun at **14**,000 rpm. for 15 min. At 3% II concentration, the precipitated fraction was fibriongen concentrate. At 8% II, the γ-globulin fraction was obtained and between 21 and 26% II, the **albumin** fraction was obtained contaminated with a trace of β-globulin. Fractionation could also be achieved at any particular I concentration by successive lowering of the temperature Fractionation was more readily achieved at lower protein concns. and precipitation proceeded

more readily at low salt concns. Optimally, protein sepns. were carried out at protein concns. of 0.4% and 20°, giving fibrinogen at 0-4% II, γ-globulin at 4-8% II, β-globulin at 8-12% II, and α-1-and α-2-globulins and **albumins** at >12% II. At pH 4.6, the γ-globulins could be optionally separated, and at pH 5.8 the β- and γ-globulins. Other proteins separated similarly were derived from Clostridium novyi **toxin**, C. **botulinum toxin** Type **D** , and pancreactic deoxyribonuclease. The prepns. of pure γ-globulin and fibrinogen are also described.

L1	1	SEA FILE=REGISTRY ABB=ON PLU=ON BOTOX/CN
L2	6	SEA FILE=REGISTRY ABB=ON PLU=ON BOTULIN TOXIN? /CN
L3	8	SEA FILE=REGISTRY ABB=ON PLU=ON BOTULIN NEUROTOXIN? /CN
L4	8	SEA FILE=REGISTRY ABB=ON PLU=ON BOTULINUM TOXIN? /CN
L5	14	SEA FILE=REGISTRY ABB=ON PLU=ON BOTULINUM NEUROTOXIN? /CN
L6	134	SEA FILE=REGISTRY ABB=ON PLU=ON (BOTULIN A ? OR BOTULIN B ? OR BOTULIN C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR BOTULIN E ? OR BOTULIN F ?)/CN
L7	2	SEA FILE=REGISTRY ABB=ON PLU=ON (BOTULINUM A ? OR BOTULINUM B ? OR BOTULINUM C1 ? OR BOTULINUM C2 ? OR BOTULINUM D ? OR BOTULINUM E ? OR BOTULINUM F ?)/CN
L8	156	SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7
L9	9	SEA FILE=REGISTRY ABB=ON PLU=ON (PHOSPHATE/CN OR "PHOSPHATE (32PO4)"/CN OR "PHOSPHATE (H2PO4-)"/CN OR "PHOSPHATE (H2PO41-)"/CN OR "PHOSPHATE (HPO42-)"/CN OR "PHOSPHATE (P2O74-)"/CN OR "PHOSPHATE (P4O123-)"/CN) OR "PHOSPHATE (P6O186-)"/CN OR ("PHOSPHATE (PO3-)"/CN OR "PHOSPHATE (PO31-)"/CN OR "PHOSPHATE (PO32-)"/CN) OR "PHOSPHATE (PO43-)"/CN OR "PHOSPHATE (PO4H2-)"/CN
L10	1	SEA FILE=REGISTRY ABB=ON PLU=ON CITRATE/CN
L11	1	SEA FILE=REGISTRY ABB=ON PLU=ON ACETATE/CN
L12	1	SEA FILE=REGISTRY ABB=ON PLU=ON SUCCINATE/CN
L13	12	SEA FILE=REGISTRY ABB=ON PLU=ON L9 OR L10 OR L11 OR L12
L15	6	SEA FILE=REGISTRY ABB=ON PLU=ON (BOTULIN G ? OR BOTULINUM G ?)/CN
L16	161	SEA FILE=REGISTRY ABB=ON PLU=ON L8 OR L15
L18	1354347	SEA FILE=HCAPLUS ABB=ON PLU=ON L13 OR PHOSPHATE OR CITRATE OR ACETATE OR SUCCINATE OR SUCCINIC OR BUTANEDIOIC OR ACETIC
L21	3	SEA FILE=REGISTRY ABB=ON PLU=ON HUMAN SERUM ALBUMIN ?/CN
L22	62	SEA FILE=REGISTRY ABB=ON PLU=ON SERUM ALBUMIN ?/CN
L23	1	SEA FILE=REGISTRY ABB=ON PLU=ON GELATINS/CN
L24	66	SEA FILE=REGISTRY ABB=ON PLU=ON L21 OR L22 OR L23
L27	6302	SEA FILE=HCAPLUS ABB=ON PLU=ON L16 OR (BO OR BOTULIN?)(5A)(NT OR TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR BOTX# OR BTX# OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(3A)(A OR B OR C1 OR C2 OR D OR E OR F OR G)
L28	290	SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L18
L29	66	SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND (14 OR NACL OR (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALINE)
L30	8	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND (L24 OR HSA OR ALBUMIN OR GELATIN)
L31	0	L30 NOT L26

should read "L14"
See L58-L65

Searcher : Shears 571-272-2528

FILE 'MEDLINE' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'BIOSIS' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'EMBASE' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'WPIDS' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'JICST-EPLUS' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'JAPIO' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'PHIC' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'PHIN' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'TOXCENTER' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'PASCAL' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'FEDRIP' ENTERED AT 11:55:55 ON 27 OCT 2005

FILE 'DISSABS' ENTERED AT 11:55:55 ON 27 OCT 2005

L32 16 S L30
L33 11 DUP REM L32 (5 DUPLICATES REMOVED)

L33 ANSWER 1 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-151958 [16] WPIDS
DOC. NO. CPI: C2005-049081
TITLE: New benzodiazepine derivatives are calcitonin gene-related peptide receptor antagonists useful in treatment of e.g. migraine, headache, tooth pain, inflammatory bowel disease and arthritis.
DERWENT CLASS: B02 B05
INVENTOR(S): BURGEY, C S; STUMP, C A; WILLIAMS, T M
PATENT ASSIGNEE(S): (MERI) MERCK & CO INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005000807	A2	20050106	(200516)*	EN	86

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT

KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005000807	A2	WO 2004-US20206	20040624

PRIORITY APPLN. INFO: US 2003-482674P 20030626
AN 2005-151958 [16] WPIDS
AB WO2005000807 A UPAB: 20050308
NOVELTY - A benzodiazepine derivative or its salt or individual diastereomer is new.

DETAILED DESCRIPTION - A benzodiazepine derivative of formula (I) or its salt or individual diastereomer is new;

R1 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, heterocycle, (hetero)aryl (all optionally substituted by at least one T) or H;

T = (hetero)aryl, heterocycle (both optionally mono- - penta-substituted by R4), 1-6C alkyl, 3-6C cycloalkyl, (F)p-1-3C alkyl, halo, OR4, O(CH2)sOR4, CO2R4, CONR10R11, O(CO)NR10R11, N(R4)CONR10R11, N(R10)(CO)R11, N(R10)(CO)OR11, SO2NR10R11, N(R10)SO2R11, S(O)mR10, CN, NR10R11, N(R10)(CO)NR4R11 or O(CO)R4;

R2 and R6 = T or H;

R7 = 0-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, heterocycle, (hetero)aryl (all optionally substituted by at least one T) or H;

R4, R10 and R11 = 1-6C alkyl, (F)p-1-6C alkyl, 3-6C cycloalkyl, (hetero)aryl, benzyl (all optionally substituted by halo, OH or 1-6C alkoxy) or H;

R5 = H, optionally substituted 1-6C alkyl, 3-6C cycloalkyl, (hetero)aryl, OR4, N(R4)2, CO2R4 or (F)p-1-6C alkyl;

W' = O, NR4 or C(R4)2;

X = C or S;

Y = O, (R4)2, NCN, NSO2CH3 or NCONH2;

R3 = H, optionally substituted 1-3C alkyl, CN or CO2R4;

R10+R11 = azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl (all optionally mono - penta-substituted by R4);

G-J = N, N-C(R5)2, C=C(R5), C=N, C(R5), C(R5)-C(R5)2, C(R5)-C(R5)2-C(R5)2, C=C(R5)-C(R5)2, C(R5)-C(R5)=C(R5), C(R5)-C(R5)2-N(R5), C=C(R5)-N(R5), C(R5)-C(R5)=N, C(R5)-N(R5)-C(R5)2, C=N-C(R5)2, C(R5)-N=C(R5), C(R5)-N(R5)-N(R5), C=N-N(R5), N-C(R5)2-C(R5)2, N-C(R5)=C(R5), N-C(R5)2-N(R5), N-C(R5)=N, N-N(R5)-C(R5)2 or N-N=C(R5);

p = 0 - 2q+1 (for substituent with q carbons);

m = 0 - 2;

n = 0 or 1;

s = 1 - 3.

Provided that when X is S, Y is O2.

An INDEPENDENT CLAIM is included for treating or preventing migraine headache, cluster headache and headache involving co-administering (I) or its salt and a second agent (A) selected from

serotonin agonist, analgesic, anti-inflammatory agent, anti-hypertensive and anticonvulsants; a second agent (B) selected from anti-anxiety agents and neuroleptics; a second agent (C) selected from beta -blockers and calcium channel blockers; a second agent (D) selected from antidepressant, selective serotonin reuptake inhibitor and NE uptake inhibitor; a second agent selected from **botulinum toxin A** or **B**; a second agent (E) selected from vanilloid receptor antagonists, adenosine 1 antagonists, NR2B antagonists, substance P antagonists, granzyme B inhibitors, endothelin antagonists, norepinephrin precursors, nitric oxide synthase inhibitors, neuroleptics, bradykinin antagonists, gap junction inhibitors, AMPA/KA antagonists, sigma receptor agonists, chloride channel enhancers, monoamine oxidase inhibitors, opioid agonists, and leukotriene receptor antagonists; or a second agent (F) selected from anti-emetics, prokinetics and histamine H1 antagonist.

ACTIVITY - Antimigraine; Analgesic; Antiinflammatory; Antidiabetic; Antiasthmatic; Antiarthritic; Antiallergic; Dermatological; Neuroprotective; Gastrointestinal-Gen.; Antipsoriatic; Vasotropic; Immunosuppressive; Antibacterial; Gynecological; Tranquilizer; Vulnerary; Anticonvulsant.

MECHANISM OF ACTION - Calcitonin Gene-related peptide (CGRP) receptor antagonist. N-((3R)-1-Ethyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-3-yl)-4-(2-oxo-1,4-dihydroquinazolin-3(2H)-yl)piperidine-1-carboxamide (A1) was tested for CGRP receptor antagonistic activity using recombinant receptor functional assay. Cells were plated in complete growth medium ar 85000 cells/well in 96-well poly-D-lysine coated plates and cultured for -19 hours. Cells were washed with **phosphate** buffered **saline** (PBS) and then incubated with (A1) for 30 minutes at 37 deg. C and 95% humidity in Cellgro Complete Serum-Free/Low Protein medium with L-glutamine and bovine serum **albumin** (1 g/l). Human alpha -CGRP was added to the cells at 0.3 nM and incubated at 37 deg. C for 5 minutes. After alpha -CGRP stimulation, the cells were washed with PBS and processed for cAMP determination according to manufacturer's recommended protocol. (A1) Showed IC50 of less than 50 micro M.

USE - For antagonizing CGRP receptor activity in a mammal; in the treatment, control, amelioration or reduction of risk of e.g. headache, migraine, cluster headache (claimed), chronic tension type headache, pain, chronic pain, neurogenic inflammation and inflammatory pain, neuropathic pain, tooth pain, diabetes, non-insulin dependent diabetes mellitus, vascular disorder, inflammation, arthritis, bronchial hyper reactivity, asthma, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, hot flushes, allergic dermatitis, psoriasis, encephalitis, brain trauma, epilepsy, neurodegenerative disease, skin disease, neurogenic cutaneous redness, skin rosaceousness and erythema, inflammatory bowel disease, irritable bowel disease and cystitis.

ADVANTAGE - The compound is potent calcitonin gene-related peptide receptor antagonist and treats CGRP receptor related disease with minimal side effects.

Dwg.0/0

L33 ANSWER 2 OF 11 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005272780 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15869543
TITLE: Pilot study of the safety and efficacy of Myobloc (**botulinum toxin** type **B**) for treatment of axillary hyperhidrosis.
AUTHOR: Baumann Leslie; Slezinger Anele; Halem Monica; Vujevich

Justin; Martin Lucy K; Black Laura; Bryde Joy
CORPORATE SOURCE: Department of Dermatology and Cutaneous Surgery, Division of Cosmetic Dermatology, University of Miami School of Medicine, 1295 NW 14th Street, South Building Suite K., Miami, FL 33125, USA.. lsb@derm.net
SOURCE: International journal of dermatology, (2005 May) 44 (5) 418-24.
Journal code: 0243704. ISSN: 0011-9059.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20050527
Last Updated on STN: 20050803
Entered Medline: 20050802

AB BACKGROUND: **Botulinum toxin** type **B** (**BTX**-B, Myobloc, San Francisco, CA, USA) was FDA-approved for the treatment of cervical dystonia in December 2000. It has since been used off-label for the treatment of axillary hyperhidrosis. However, there are sparse data in the medical literature evaluating the safety and efficacy of Myobloc (**botulinum toxin** type **B**) for this indication. OBJECTIVE: To assess the safety, efficacy and duration of action of Myobloc (**botulinum toxin** type **B**) in the treatment of bilateral axillary hyperhidrosis. METHODS: This study was a double-blinded, randomized, pilot study conducted in an outpatient office setting at a private academic medical center beginning in November 2001. Twenty-three male and female volunteers between the ages of 18 and 80 were screened for participation; 20 participants with primary axillary hyperhidrosis were enrolled. Participants were injected subcutaneously with either Myobloc (**botulinum toxin** type **B**) (2500 U, or 0.5 ml, per axilla) or 0.5 ml vehicle (100 mM **NaCl**, 10 mM **succinate**, and 0.5 mg/ml human **albumin**) into bilateral axillae. Participants who received placebo were rolled over and received Myobloc (**botulinum toxin** type **B**) at subsequent visits. All participants were followed until sweating returned to baseline levels. This trial was initially conceived as a placebo-controlled study; however, owing to the insufficient size of the placebo group, the placebo arm of this trial was dropped during data analysis. The main outcome measures were safety, efficacy, and duration of effect. RESULTS: According to participant assessment of axillary hyperhidrosis improvement (A-HI) and quality of life (A-HQOL) scores and the physician assessment scores, a significant difference was observed in treatment response at Day 30 in the participants receiving Myobloc (**botulinum toxin** type **B**) injections. Duration of action ranged from 2.2 to 8.1 months (mean 5.0 months). The adverse event profile included bruising, flu-like symptoms, and dry eyes. CONCLUSION: Myobloc (**botulinum toxin** type **B**) proved to be safe and efficacious for the treatment of bilateral axillary hyperhidrosis. More studies are needed to assess the duration of response using different doses of Myobloc (**botulinum toxin** type **B**).

L33 ANSWER 3 OF 11 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005207480 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15841624
TITLE: Double-blind, randomized, placebo-controlled pilot study of the safety and efficacy of Myobloc (**botulinum toxin** type **B**) for the treatment of palmar hyperhidrosis.
COMMENT: Comment in: Dermatol Surg. 2005 Sep;31(9 Pt 1):1158. PubMed ID: 16164873
AUTHOR: Baumann Leslie; Slezinger Anele; Halem Monica; Vujevich Justin; Mallin Karin; Charles Carlos; Martin Lucy K; Black Laura; Bryde Joy
CORPORATE SOURCE: Department of Dermatology and Cutaneous Surgery/Division of Cosmetic Dermatology, University of Miami, Miami, Florida, USA.. lsb@derm.net
SOURCE: Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.], (2005 Mar) 31 (3) 263-70.
Journal code: 9504371. ISSN: 1076-0512.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050422
Last Updated on STN: 20050513
Entered Medline: 20050512

AB BACKGROUND: Palmar hyperhidrosis is a problem of unknown etiology that affects patients both socially and professionally. **Botulinum toxin** type **B** (Myobloc), approved by the Food and Drug Administration for use in the treatment of cervical dystonia in the United States in December 2000, has subsequently been used effectively in an off-label indication to treat hyperhidrosis. There are sparse data, however, in the literature evaluating the safety and efficacy of **BTX**-B for the treatment of palmar hyperhidrosis. OBJECTIVE: We evaluated the safety and efficacy of Myobloc in the treatment of bilateral palmar hyperhidrosis. This was a double-blind, randomized, placebo-controlled study to report on the safety and efficacy of Myobloc. METHODS: Twenty participants (10 men, 10 women) diagnosed with palmar hyperhidrosis were injected with either Myobloc (5,000 U per palm) or a 1.0 mL vehicle (100 mM **NaCl**, 10 mM **succinate**, and 0.5 mg/mL human **albumin**) into bilateral palms (15 Myobloc, 5 placebo). The participants were followed until sweating returned to baseline levels. The main outcome measures were safety, efficacy versus placebo, and duration of effect. RESULTS: A significant difference was found in treatment response at day 30, as determined by participant assessments, between 15 participants injected with Myobloc and 3 participants injected with placebo. The duration of action, calculated in the 17 participants who received Myobloc injections and completed the study, ranged from 2.3 to 4.9 months, with a mean duration of 3.8 months. The single most reported adverse event was dry mouth or throat, which was reported by 18 of 20 participants. The adverse event profile also included indigestion or heartburn (60%), excessively dry hands (60%), muscle weakness (60%), and decreased grip strength (50%). CONCLUSION: Myobloc proved to be efficacious for the treatment of palmar hyperhidrosis. Myobloc had a rapid onset, with most participants responding within 1 week. The duration of action ranged from 2.3 to 4.9 months, with a mean of 3.8 months. The adverse event profile

included dry mouth, indigestion or heartburn, excessively dry hands, muscle weakness, and decreased grip strength.

L33 ANSWER 4 OF 11 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:288014 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA14001008814Y
TITLE: Pharmaceutical preparation of **botulinum neurotoxin**
AUTHOR(S): Zabudkin, Alexander F.; Krasnopolsky, Juri M.; Itkin, Aleksandr M.; Itkin, Dmitry M.
PATENT INFORMATION: US 2003224020 A1 4 Dec 2003
SOURCE: (2003) U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO.
COUNTRY: UKRAINE
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:950462
LANGUAGE: English
ENTRY DATE: Entered STN: 20031209
Last Updated on STN: 20050524

AB **A** pharmaceutical preparation of **botulinum neurotoxins** free of human blood products (such as human **albumin**), the preparation comprising **a botulinum neurotoxin** incorporated in phosphatidylcholine liposomes. A flask is filled with a solution of phosphatidylcholine in ethanol containing 0.1 g lipid. The solution is subjected to evaporation at 35° until a lipid film is formed. He lipid film is then resuspended in 10-L sterile 0.9% **sodium chloride** solution with 7.0-7.4 **phosphate** buffer containing 1 mg of **botulinum** type **A neurotoxin** complex (95-98% purity). After the lipid film is successfully resuspended from the flask walls, the resulting emulsion is thoroughly mixed for 30 min until homogeneous emulsion is produced. Such emulsion is then transferred into a homogenizing reactor and the emulsion is homogenized at a pressure of 60 MPa and a temperature of 30-35°. When an optical d. of 0.1-0.12 is achieved, 25 g lactose is added to the emulsion. The resulting emulsion is then sequentially filtered. The resulting sterile emulsion is then distributed into vials or ampuls, each containing 0.1 mL sterile emulsion. The vials or ampuls are deep frozen at -70° for 48 h, followed by lyophilization. After lyophilization, the vials are hermetically sealed with an atmospheric of inert gas introduced over the lyophilized emulsion in the vial.

L33 ANSWER 5 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-164340 [21] WPIDS
DOC. NO. CPI: C2002-050729
TITLE: Immunoconjugate for increasing anti-tumor activity of immunotoxin, has a connector molecule attaching a targeting molecule to an effector molecule, conjugated to one or more polyethylene glycol molecules.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): LEE, B; NAGATA, S; ONDA, M; PASTAN, I H; TSUTSUMI, Y; PASTAN, H; KREITMAN, R J; PASTAN, I
PATENT ASSIGNEE(S): (KREI-I) KREITMAN R J; (USSH) US DEPT HEALTH & HUMAN SERVICES; (LEEB-I) LEE B; (NAGA-I) NAGATA S; (ONDA-I) ONDA M; (PAST-I) PASTAN I; (TSUT-I) TSUTSUMI Y
COUNTRY COUNT: 97

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001095942	A2	20011220	(200221)*	EN	58
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001069762	A	20011224	(200227)		
EP 1351709	A2	20031015	(200368)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					
JP 2004503512	W	20040205	(200412)		105
US 2004018203	A1	20040129	(200413)		
EP 1351709	B1	20040915	(200460)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					
DE 60105647	E	20041021	(200469)		
EP 1351709	B8	20041222	(200501)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					
ES 2228903	T3	20050416	(200528)		
AU 2001269762	B2	20050623	(200545)		
DE 60105647	T2	20050922	(200562)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001095942	A2	WO 2001-US18503	20010608
AU 2001069762	A	AU 2001-69762	20010608
EP 1351709	A2	EP 2001-948294	20010608
		WO 2001-US18503	20010608
JP 2004503512	W	WO 2001-US18503	20010608
		JP 2002-510119	20010608
US 2004018203	A1	WO 2001-US18503	20010608
		US 2002-297337	20021204
EP 1351709	B1	EP 2001-948294	20010608
		WO 2001-US18503	20010608
DE 60105647	E	DE 2001-00105647	20010608
		EP 2001-948294	20010608
		WO 2001-US18503	20010608
EP 1351709	B8	EP 2001-948294	20010608
		WO 2001-US18503	20010608
ES 2228903	T3	EP 2001-948294	20010608
AU 2001269762	B2	AU 2001-269762	20010608
DE 60105647	T2	DE 2001-00105647	20010608
		EP 2001-948294	20010608
		WO 2001-US18503	20010608

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001069762	A	Based on	WO 2001095942
EP 1351709	A2	Based on	WO 2001095942
JP 2004503512	W	Based on	WO 2001095942
EP 1351709	B1	Based on	WO 2001095942

Searcher : Shears 571-272-2528

DE 60105647	E	Based on	EP 1351709
		Based on	WO 2001095942
EP 1351709	B8	Based on	WO 2001095942
ES 2228903	T3	Based on	EP 1351709
AU 2001269762	B2	Previous Publ.	AU 2001269762
		Based on	WO 2001095942
DE 60105647	T2	Based on	EP 1351709
		Based on	WO 2001095942

PRIORITY APPLN. INFO: US 2000-213804P 20000622; US 2000-211331P 20000609; US 2002-297337 20021204

AN 2002-164340 [21] WPIDS

AB WO 200195942 A UPAB: 20020403

NOVELTY - A composition (I) comprising a targeting molecule linked to an effector molecule through a connector molecule, and one or more polyethylene glycol (PEG) molecules conjugated to the connector molecule, is new.

ACTIVITY - Cytostatic.

To assess antitumor activity, ATac-4 cells were inoculated subcutaneously in nude mice on day 0. Treatment was started on day 4 when the tumors measured about 100 mm3. Animals were treated intravenously with 3 doses given on days 4, 6 and 8. The control groups received vehicle (**phosphate** buffered **saline** (PBS) containing 0.2 % bovine serum **albumin** (BSA)) or 10 micro g of PEG5K or PEG20K. Native and mutant anti-Tac(Fv)-PE38 (LMB-2) inhibited tumor growth in a dose-dependent manner. Complete regressions, which were defined as disappearance of tumor without regrowth after more than 50 days, were observed in 2 of 5 mice or 1 of 5 mice at the dose of 0.1 mg/kg multiply 3 of native or mutant LMB-2, respectively. At 0.2 mg/kg multiply 3 dose level one of 5 mice administered either native or mutant LMB-2 died from toxicity during the therapeutic period, but complete regressions were observed in all four remaining mice. The antitumor activities of both types of PEGylated LMB-2s were markedly improved. Complete regression was observed in 1 of 5 mice or 2 of 5 mice at the dose of 0.025 mg/kg multiply 3 of PEG5K- or PEG20K-LMB-2, respectively. At the dose of 0.05 mg/kg multiply 3, PEGylated LMB-2s caused complete regressions lasting over 50 days. Both types of PEGylated LMB-2 showed a 3-4-fold higher anti-tumor activity than unmodified native and mutant LMB-2. In addition, their toxicity to mice was reduced about 6-fold. PEGylation led to a 20-fold increase in therapeutic efficacy, increased LMB-2 blood-residence, which was due to an increase in molecular size and enhanced stability. The plasma half-lives were 5-fold longer with PEG5K-LMB-2 and 8-fold longer with PEG20K-LMB-2 than with unmodified LMB-2s.

MECHANISM OF ACTION - Inhibits or kills growth of target cells.

USE - (I) having a targeting moiety and a toxin moiety connected by a connector molecule, where two or more amino acid residues of the connector molecule are conjugated to PEG, is useful for increasing anti-tumor activity of an immunotoxin (claimed). The immunotoxins selectively inhibit or kill cells to which the immunotoxins are targeted by the targeting moiety. They kill or inhibit the growth of cells of CD25+ hematologic malignancies, including e.g. hairy cell leukemia (HCL), cutaneous T-cell lymphoma, chronic lymphocytic leukemia, Hodgkin's disease and adult T-cell leukemia and in vivo inhibit the growth of malignant cells in an organism.

ADVANTAGE - The PEGylated immunotoxin has comparable in vitro specific cytotoxicity against tumor cells, and improved stability,

plasma half-life, antitumor activity, immunogenicity and non-specific toxicity. The PEGylation of the linker or connector portion of an immunotoxin increases the anti-tumor activity of the immunotoxin, while decreasing its toxicity and immunogenicity.
Dwg.0/6

L33 ANSWER 6 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 3
ACCESSION NUMBER: 2000-271251 [23] WPIDS
DOC. NO. CPI: C2000-082761
TITLE: Stable liquid pharmaceutical **botulinum toxin** formulation, useful for treating spasticity due to stroke, spinal cord injury, closed head trauma, cerebal palsy, multiple sclerosis, or Parkinson's disease.
DERWENT CLASS: B04
INVENTOR(S): HIRTZER, P; MOYER, E
PATENT ASSIGNEE(S): (ELAN-N) ELAN PHARM INC
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000015245	A2	20000323	(200023)*	EN	34
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9958214	A	20000403	(200034)		
NO 2001001207	A	20010509	(200134)		
BR 9913585	A	20010605	(200138)		
CZ 2001000564	A3	20010613	(200138)		
EP 1112082	A2	20010704	(200138)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SK 2001000313	A3	20011008	(200163)		
CN 1316906	A	20011010	(200207)		
KR 2001086388	A	20010910	(200219)		
HU 2001003638	A2	20020128	(200222)		
EP 1112082	B1	20020731	(200257)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
DE 69902396	E	20020905	(200266)		
JP 2002524527	W	20020806	(200266)		46
AU 755556	B	20021212	(200305)		
ES 2181473	T3	20030216	(200321)		
ZA 2001001709	A	20030226	(200321)		51
NZ 509349	A	20030829	(200365)		
MX 2001002445	A1	20021001	(200370)		
TW 574036	A	20040201	(200453)		
IN 2001000165	P2	20050311	(200555)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000015245	A2	WO 1999-US20912	19990909
AU 9958214	A	AU 1999-58214	19990909

NO 2001001207	A	WO 1999-US20912	19990909
		NO 2001-1207	20010309
BR 9913585	A	BR 1999-13585	19990909
		WO 1999-US20912	19990909
CZ 2001000564	A3	WO 1999-US20912	19990909
		CZ 2001-564	19990909
EP 1112082	A2	EP 1999-945649	19990909
		WO 1999-US20912	19990909
SK 2001000313	A3	WO 1999-US20912	19990909
		SK 2001-313	19990909
CN 1316906	A	CN 1999-810739	19990909
KR 2001086388	A	KR 2001-703032	20010309
HU 2001003638	A2	WO 1999-US20912	19990909
		HU 2001-3638	19990909
EP 1112082	B1	EP 1999-945649	19990909
		WO 1999-US20912	19990909
DE 69902396	E	DE 1999-602396	19990909
		EP 1999-945649	19990909
		WO 1999-US20912	19990909
JP 2002524527	W	WO 1999-US20912	19990909
		JP 2000-569829	19990909
AU 755556	B	AU 1999-58214	19990909
ES 2181473	T3	EP 1999-945649	19990909
ZA 2001001709	A	ZA 2001-1709	20010228
NZ 509349	A	NZ 1999-509349	19990909
		WO 1999-US20912	19990909
MX 2001002445	A1	WO 1999-US20912	19990909
		MX 2001-2445	20010308
TW 574036	A	TW 1999-114941	19990831
IN 2001000165	P2	WO 1999-US20912	19990909
		IN 2001-KN165	20010313

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9958214	A	Based on	WO 2000015245
BR 9913585	A	Based on	WO 2000015245
CZ 2001000564	A3	Based on	WO 2000015245
EP 1112082	A2	Based on	WO 2000015245
SK 2001000313	A3	Based on	WO 2000015245
HU 2001003638	A2	Based on	WO 2000015245
EP 1112082	B1	Based on	WO 2000015245
DE 69902396	E	Based on	EP 1112082
		Based on	WO 2000015245
JP 2002524527	W	Based on	WO 2000015245
AU 755556	B	Previous Publ.	AU 9958214
		Based on	WO 2000015245
ES 2181473	T3	Based on	EP 1112082
NZ 509349	A	Based on	WO 2000015245
MX 2001002445	A1	Based on	WO 2000015245

PRIORITY APPLN. INFO: US 1998-99870P 19980911

AN 2000-271251 [23] WPIDS

AB WO 200015245 A UPAB: 20000516

NOVELTY - **A** stable liquid pharmaceutical **botulinum toxin** formulation (I), comprising a buffer giving a pH range of 5 to 6 and isolated **botulinum toxin**, stable at a temperature of 0 to 30 deg. C for at least 1 year, is new.

Searcher : Shears 571-272-2528

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of treating a patient requiring inhibition of cholinergic input to a muscle, gland, or organ comprising administering (I).

ACTIVITY - Relaxant; cerebroprotective; neuroprotective; antiparkinsonian; analgesic; antimigraine; antiasthmatic.

Twenty-eight patients with a mean age of 50.9 with a confirmed diagnosis of cervical dystonia, received injections of **botulinum toxin** Type **B** formulation into 2-4 superficial neck and shoulder muscles with escalating doses (up to 1.5 fold per successive session) over time. Clinical benefit was assessed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Severity test, with 25% reduction in score considered an improvement. Patients participated in the study from 28 to 177 days with a mean time in the study of 71.9 days. Patients were treated with 1 to 3 doses of formulation. Cumulative doses ranged from 1430 U to 12000 U, with individual doses ranging from 300 U to 12000 U. For purposes of clinical assessment, 4 dose groups were defined: 100-800 U (Group A), 900-2399 U (Group B), 2400-5999 U (Group C), and 6000-12000 U (Group D). The length of time between dosing sessions ranged as follows: Group A, 13-101 days; Group B, **14**-113 days; Group C, 29-177 days; and Group D, 28-177 days. Mean baseline scores were similar in all patients in all treatment groups, and all 4 groups experienced a mean decrease in score (improvement) during the study. Overall, mean percent improvement from baseline and mean response ratio for severity score was greatest in Groups C and D during the study. Measures of mean maximum improvement, mean maximum percent improvement and mean maximum response ratio were greater for the two higher dose groups (8.1 and 6.8 against 2.1 and 3.6 for maximum improvement). The percentage of patients responding to treatment was greater for the two higher dose groups (80 and 78% for C and D, respectively compared to 0 and 27% for A and B, respectively). The results therefore showed a dose-dependent response to **botulinum B toxin** formulations.

MECHANISM OF ACTION - (I) inhibits cholinergic input into muscles, glands and organs.

USE - The composition is useful for treating spasticity (due to stroke, spinal cord injury, closed head trauma, cerebal palsy, multiple sclerosis, or Parkinson's), blepharospasm, strabismus, hemifacial spasm, dystonia, otitis media, spastic colitis, anismus, urinary detrusor-sphincter dyssynergia, jaw-clenching, and curvature of the spine. (I) is also useful for treatment of myofascial pain, headache associated with migraine, vascular disturbances, neuralgia, neuropathy, arthrotos pain, back pain, hyperhydrosis, rhinnorhea, asthma, excessive salivation, and excessive stomach acid secretion.

Dwg.0/0

L33 ANSWER 7 OF 11 EMBASE

ACCESSION NUMBER: 2000272711 EMBASE
TITLE: **Botox** and dysport are distinct (multiple letters).
AUTHOR: Madalinski M.; Thumshirn M.
CORPORATE SOURCE: M. Madalinski, ul. Kosciuszki 101-7, 80-421 Gdansk, Poland. m.h.madalinski@pro.onet.pl
SOURCE: Endoscopy, (2000) Vol. 32, No. 6, pp. 502-503.
Refs: 0
ISSN: 0013-726X CODEN: ENDCAM
COUNTRY: Germany
DOCUMENT TYPE: Journal; Letter

FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 20000817
Last Updated on STN: 20000817
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L33 ANSWER 8 OF 11 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:185698 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12123274169N
TITLE: Recovery of type **A botulinal toxin** following lyophilization
AUTHOR(S): Goodnough, Michael C.; Johnson, Eric A.
CORPORATE SOURCE: Food Res. Inst., Univ. Wisconsin, Madison, WI, 53706, USA.
SOURCE: ACS Symposium Series, (1994) Vol. 567, No. Formulation and Delivery of Proteins and Peptides, pp. 193-203.
CODEN: ACSMC8. ISSN: 0097-6156.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1994:674169
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020910

AB Type **A botulinum toxin** is diluted to very low concns. (ng/mL) for medical use and preserved by lyophilization in a mixture of human serum **albumin** and **sodium chloride** at a slightly alkaline pH. This com. process results in considerable loss of activity. In this study, conditions were found that gave >90% recovery of the toxicity following lyophilization of solns. containing 20-1000 mouse 50% LDs (1-50 ng of toxin complex). Full recovery of starting toxicity was obtained upon drying 0.1 mL when the pH was maintained below 7.0 and serum **albumins** or other protein excipients were used as stabilizers without **sodium chloride**. Possible mechanisms of toxin inactivation were examined and may include aggregation, deamidation, and peptide bond hydrolysis.

L33 ANSWER 9 OF 11 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:172428 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA11724239677X
TITLE: Stabilization of **botulinum toxin** type **A** during lyophilization
AUTHOR(S): Goodnough, Michael C.; Johnson, Eric A.
CORPORATE SOURCE: Dep. Food Microbiol. Toxicol., Univ. Wisconsin, Madison, WI, 53706, USA.
SOURCE: Applied and Environmental Microbiology, (1992) Vol. 58, No. 10, pp. 3426-8.
CODEN: AEMIDF. ISSN: 0099-2240.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1992:639677

LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021001

AB **Botulinum toxin** for medical use is diluted to very low concns. (nanograms per mL); when it is preserved by lyophilization, considerable loss of activity can occur. In the present study, conditions that gave >90% recovery of the toxicity after lyophilization of solns. containing 20 to 1000 mouse 50% LDs per mL were found. Toxicity was recovered upon drying 0.1 mL of toxin solution when the pH was maintained below 7 and bovine or human serum **albumins** were used as stabilizers. Various other substances tested with **albumin**, including glucose, sucrose, trehalose, mannitol, glycine, and cellobiose, did not increase recovery on drying.

L33 ANSWER 10 OF 11 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:34791 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA06413107065Y
TITLE: The effect of temperature on toxin formation and **toxin** stability of Clostridium **botulinumn** type **E** in different environments
AUTHOR(S): Abrahamsson, Kerstin; Gullmar, B.; Molin, N.
CORPORATE SOURCE: Swedish Inst. Food Preserv. Res., Goteborg.
SOURCE: Canadian Journal of Microbiology, (1966) Vol. 12, No. 2, pp. 385-94.
CODEN: CJMIAZ. ISSN: 0008-4166.
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1966:107065
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20030513

AB C. **botulinum** type **E** produced **toxin** at temps. between 3° and 30° in a chopped meat medium and in a fish dialyzate. The toxin was produced more rapidly in the meat medium. No toxin was found after 1 year of incubation at 1°. At 3°, slight toxin production was noticed after 120 days, when the inoculum consisted of a mixture of vegetative cells and spores. The lowest concentration of **NaCl** necessary to inhibit toxin production varied with the incubation temperature and duration of storage. The inhibiting effect of **NaCl** was more pronounced at a lower temperature Type E spores mixed in fish-meat medium heated for 110 min. at 80° or for 10 min. at 90° produced toxin during prolonged storage at 20% but not after they were heated at 90° for 20 min. Toxin (type E) proved more thermostable in meat broth and fish dialyzate than in **phosphate** buffer solution or in buffer supplemented with **gelatin**. In meat broth, the toxin was inactivated after 5 min. at 65°.

L33 ANSWER 11 OF 11 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:29482 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA06401005105U
TITLE: Fractionation of proteins in an aqueous medium
AUTHOR(S): Polson, Alfred
CORPORATE SOURCE: ASSIGNEE: South African Inventions Development Corp.
PATENT INFORMATION: GB 1006258 29 Sep 1965

SOURCE: (1965)
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1966:5105
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20040511

AB A process is described for rendering less soluble or less dispersible in an aqueous liquid a proteinaceous substance by addition of a polyethylene glycol (I) of mol. weight 1500-20,000. The process is useful for fractionating and purifying various types of protein. Human plasma was diluted with an equal volume of H2O, giving a protein concentration of 3.8% by weight Portions of this soluble (5 ml.) were added to 5-ml. proteins of I (mol. weight 6000) (II) of increasing concentration dissolved in a 1/3M **phosphate** buffer of pH 7.0. The mixts. were kept at 21° for 30 min. then spun at **14**,000 rpm. for 15 min. At 3% II concentration, the precipitated fraction was fibriongen concentrate. At 8% II, the γ-globulin fraction was obtained and between 21 and 26% II, the **albumin** fraction was obtained contaminated with a trace of β-globulin. Fractionation could also be achieved at any particular I concentration by successive lowering of the temperature Fractionation was more readily achieved at lower protein concns. and precipitation proceeded more readily at low salt concns. Optimally, protein sepns. were carried out at protein concns. of 0.4% and 20°, giving fibrinogen at 0-4% II, γ-globulin at 4-8% II, β-globulin at 8-12% II, and α-1-and α-2-globulins and **albumins** at >12% II. At pH 4.6, the γ-globulins could be optionally separated, and at pH 5.8 the β- and γ-globulins. Other proteins separated similarly were derived from Clostridium novyi **toxin**, C. **botulinum toxin** Type **D** , and pancreactic deoxyribonuclease. The prepns. of pure γ-globulin and fibrinogen are also described.

FILE 'HCAPLUS' ENTERED AT 11:59:55 ON 27 OCT 2005
L34 22 S L29 AND BUFFER?
L35 16 S L29 AND (TEMP OR TEMPERATURE)
L36 28 S (L34 OR L35) NOT L30

L36 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:983609 HCAPLUS
DOCUMENT NUMBER: 143:272525
TITLE: Composition and methods for topical application and transdermal delivery of **botulinum toxin**
INVENTOR(S): Dake, Michael D.; Waugh, Jacob M.
PATENT ASSIGNEE(S): Essentia Biosystems, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005196414	A1	20050908	US 2005-72026	20050303

WO 2005084410 A2 20050915 WO 2005-US7524 20050303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-550015P P 20040303

AB A composition for topical application of **a botulinum toxin** (including **botulinum toxin** derivs.) comprises **a botulinum toxin** and **a** carrier comprising a polymeric backbone having attached pos. charged branching groups. The invention also relates to methods for reducing muscle paralysis and other conditions that may be treated with **a botulinum toxin**, particularly paralysis of s.c., and most particularly, facial, muscles, by topically applying an effective amount of the **botulinum toxin** and carrier, in conjunction, to the subject's skin or epithelium. Kits for administration are also described. For example, topical **botulinum toxin** with **a** peptidyl carrier was prepared The pos. charged backbone was assembled by conjugating -Gly3Arg7 to polylysine (MW 112,000) via the carboxy of the terminal glycine to free amines of the lysine side chains at a degree of saturation of 18 % (i.e., 18 out of each 100 lysine residues is conjugated to a -Gly3Arg7). An aliquot of **botulinum toxin A** was biotinylated with a calculated 12-fold molar excess of sulfo-NHS-LC biotin. Biotinylated **botulinum toxin A** 2.0 unit per aliquot (i.e. 20 U total) and peptidyl carrier at a calculated MW ratio of 4:1 were mixed to homogeneity and diluted to 600 μL with **phosphate buffered saline**. The resulting composition was mixed to homogeneity with 5.4 mL of Cetaphil and aliquoted in 200 μL portions. Topical application of above composition demonstrated that the peptidyl carrier can transport a therapeutically effective amount of **botulinum toxin** across skin without covalent modification of the therapeutic.

L36 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1003887 HCAPLUS
DOCUMENT NUMBER: 142:128923
TITLE: Factors Affecting Autocatalysis of **Botulinum A Neurotoxin** Light Chain
AUTHOR(S): Ashraf Ahmed, S.; Ludivico, Matthew L.; Smith, Leonard A.
CORPORATE SOURCE: Department of Immunology and Molecular Biology, Division of Toxinology and Aerobiology, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, 21702, USA
SOURCE: Protein Journal (2004), 23(7), 445-451
CODEN: PJROAH; ISSN: 1572-3887
PUBLISHER: Springer Science+Business Media, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The light chain of **botulinum neurotoxin** serotype **A** undergoes autocatalytic fragmentation into two major peptides during purification and storage by both intermol. and intramol. mechanisms. In this study, the authors investigated the effects of **buffers** and salts on this autocatalytic reaction in the presence and absence of zinc chloride. In the presence of zinc chloride, the fragmentation reaction was enhanced in each of **acetate**, MES, HEPES and **phosphate buffers** with maximum occurring in **acetate** when compared to those in the absence of zinc chloride. Adding **sodium chloride** in **phosphate buffer** in the presence of zinc chloride increased the extent of proteolysis. Irresp. of the presence of zinc chloride, adding **sodium chloride** or potassium chloride in **phosphate buffer** elicited an addnl. proteolytic reaction. Higher concns. of sodium **phosphate buffer** enhanced the autocatalytic reaction in the absence of zinc chloride. In contrast, in the presence of zinc chloride, higher concns. of sodium **phosphate** decreased the autocatalytic reaction. Optimum pH of autocatalysis was not affected significantly by the absence or presence of zinc chloride. Like zinc chloride, other chlorides of divalent metals, such as magnesium, cobalt, iron and calcium also enhanced the autocatalytic reaction. Polyols such as ethylene glycol protected the light chain from fragmentation. Exposure of light chain to UV radiation led to enhanced fragmentation. To avoid fragmentation, the protein should be stored frozen in a low concentration **buffer** of neutral or higher pH devoid of any metal. The authors' results provide a choice of **buffers** and salts for isolation, purification and storage of intact **botulinum neurotoxin** serotype **A** light chain.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:905843 HCAPLUS
DOCUMENT NUMBER: 141:6042
TITLE: Combined effects of ionizing-irradiation and different environments on Clostridium **botulinum** type **E** spores
AUTHOR(S): Lim, Y. H.; Hamdy, M. K.; Toledo, R. T.
CORPORATE SOURCE: Department of Food Science and Technology, University of Georgia, Athens, GA, 30602, USA
SOURCE: International Journal of Food Microbiology (2003), 89(2-3), 251-263
CODEN: IJFMDD; ISSN: 0168-1605
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We examined the combined effects of γ-radiation (24 °C) on spores of Clostridium botulinum-type Eklund strain suspended in different gas-saturated Na-**phosphate buffers** in the absence or presence of protectors or sensitizers. Response surface methodol. (RSM) was also used to ascertain the effects of radiation on the recovery of spores using a medium containing various levels of **NaCl** or Na-thioglycolate. The former (<0.5%) decreased viable spore counts, but the latter (0.15%) did not. Irradiation inactivation of

Eklund spores was most effective in air-saturated **buffers** compared to N2O and N2 gas. The Na2-EDTA (0.01 M) was the most efficient radioprotector of spores due to its reactivity toward hydroxy radicals, followed by t-butanol (0.1 M) in NO2 or N2-saturated **buffers**, resp. Catalase (10.0 mg ml-1) and dl-cysteine (0.1 mM) sensitized the spores during irradiated N2O or N2-saturated **buffers**, and **NaCl** (0.01 M) only sensitized spores in N2 environment. Spores frozen at -75°C for 30 days and thawed prior to use were more sensitive to radiation damage compared to freshly prepared spores. Glycerol (15%), in Na-**phosphate buffer** (pH 7.0, 0.06 M), protected Eklund spores and increased the number of spores from 106 to 1011 colony forming unit (CFU) ml-1, and enhanced their radiosensitivities. Seven strains of C. **botulinum** type **E** were screened for plasmids and strain BL764 had two plasmids (15.8 and 46.8 mDa), BL4028 also had two (4.4 and 13.2 mDa), BL4850 contained only one (4.9 mDa), whereas EQA, BL211, Eklund, and Beluga had none. γ-Radiation (10 kGy, absorbed dose) cured the 15.8-mDa plasmid in strain BL764, but its absence yielded no changes in toxigenicity.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:491426 HCAPLUS
DOCUMENT NUMBER: 135:43124
TITLE: Method of immunoenzymic detection of **botulin toxin** and apparatus for the detection
INVENTOR(S): Trojan, Czeslaw; Kuczek, Marian
PATENT ASSIGNEE(S): Wyzsza Szkola Oficerska im.Tadeusza Kosciuszki, Pol.
SOURCE: Pol., 4 pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 179790	B1	20001031	PL 1994-305816	19941109
PRIORITY APPLN. INFO.:			PL 1994-305816	19941109

AB A semiquant. field method for the immunoenzymic detection of **botulin toxin** on glass fiber paper Whatman GF/A is described. Anti-botulotoxin antibodies labeled with fluorescein isothiocyanate (FITC) are fixed on the dry paper in a vertical line. The crossing horizontal line made under UV lamp contains similarly FITC-labeled antibodies with **botulin toxin** or toxoid. After drying the paper is saturated with 1% casein. On the prepared paper, a drop of the aqueous extract of the sample is applied, followed by 0.5 mL stabilized anti-botulotoxin antibodies labeled with peroxidase (1 μg/mL in 0.1 M **phosphate buffer** pH 6.5). After soaking of the solns. into the paper and drying, the paper surface is washed with 1% aqueous **NaCl** with 0.01% cetylpyrimidine HCl detergent in 0.01% **phosphate buffer** pH 6.5. Subsequently a drop of alc. solution of the chromogenic substrate (tetramethylbenzidine chloride or sulfate) and

H2O2 are added. The developed color is visually judged pos. or neg. for the **botulin toxin** presence it the sample examined A simple box device for the test execution is described.

L36 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:425354 HCAPLUS
DOCUMENT NUMBER: 131:224672
TITLE: Detection of sparse **botulinum toxin A** binding sites using fluorescent latex microspheres
AUTHOR(S): Crosland, Richard D.; Canziani, Gabriela A.
CORPORATE SOURCE: Toxinology Division, United States Army Medical Research Institute of Infectious Diseases, Frederick, MD, 21702, USA
SOURCE: Journal of Histotechnology (1999), 22(2), 113-115
CODEN: JOHIDN; ISSN: 0147-8885
PUBLISHER: National Society for Histotechnology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The most potent toxins known are produced by strains of Clostridium botulinum. To paralyze the vertebrate neuromuscular junction, the toxins bind selectively to nerve endings, translocate into the presynaptic terminal, and hydrolyze proteins of the exocytotic apparatus, thus inhibiting the release of acetylcholine. Our goal was to develop a convenient, reliable technique to detect specific binding of **botulinum toxin A** to its targets, a technique that could be easily modified to detect the binding sites of other ligands as well. Our method utilized fluorescent latex microspheres and is theor. capable of detecting a single binding site at the light microscopic level. Nonspecific binding sites on 7-μm thick sections of unfixed, cryosectioned mouse diaphragm were first blocked with 20% goat serum in **phosphate-buffered saline** (GS/PBS). We incubated the diaphragm for 1 h at 22° with various concns. of **botulinum toxin A** in GS/PBS, followed by incubation with rabbit anti-**botulinum toxin A** antiserum, biotin-labeled goat anti-rabbit antibody, and finally avidin-labeled, 0.03 μm diameter, fluorescent latex microspheres. As expected, binding was localized to the area of the neuromuscular junction. Binding was also observed in association with axons innervating some junctions. We could detect binding on diaphragms that were exposed to as little as 10 pM **botulinum toxin A**, which is in the low range of effective in vitro doses that block neuromuscular transmission. This is a convenient, sensitive, and specific technique for detecting **botulinum toxin A** binding sites that is easily modifiable for the detection of binding sites of other ligands as well.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:636107 HCAPLUS
DOCUMENT NUMBER: 127:292350
TITLE: Low-acid, high-moisture processed cheese spread and method of making
INVENTOR(S): Adrianson, Tim M.; Brown, Alpheus I., Jr.; Busk, G. Curtis, Jr.; Gunther, Stephen A.; Huether, Karen D.; Mann, Joseph W.; Yoss, James K.

PATENT ASSIGNEE(S): Nabisco, Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5670197	A	19970923	US 1995-536406	19950929
PRIORITY APPLN. INFO.:			US 1995-536406	19950929

AB High-moisture, high-pH, shelf-stable cheese spreads containing cheese, preferably a cheese having a pH of 5.4 or lower such as Swiss, Cheddar, American, mozzarella, skim milk cheese, or cheese mixts., water sufficient to provide a total moisture of from 51 to 58% and a pH of from 5.3 to 6.0 are preserved by adding **sodium chloride**, a **phosphate** salt, sodium **citrate**, and sodium lactate in sufficient amts. to maintain the composition free from the growth of Clostridium **botulinum** and the production of **toxin** by those organisms during room **temperature** storage for a period of at least 180 days, preferably 300 days. Some embodiments contain 1 to 2% sodium **citrate**, 1 to 2% sodium lactate, and a combined level of dibasic sodium **phosphate** and **sodium chloride** ranging between 1.3 and 2.2%, and have a moisture content of 52 to 55%, and an overall pH of about 5.3 to 5.6.

L36 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:998457 HCAPLUS
DOCUMENT NUMBER: 124:54039
TITLE: Growth of proteolytic Clostridium botulinum in process cheese products: I. Data acquisition for modeling the influence of pH, **sodium chloride**, emulsifying salts, fat dry basis, and **temperature**
AUTHOR(S): Ter Steeg, Pieter F.; Cuppers, Henk G. A. M.; Hellemons, Johan C.; Rijke, Guus
CORPORATE SOURCE: Unilever Research Laboratorium, Vlaardingen, 3133 AT, Neth.
SOURCE: Journal of Food Protection (1995), 58(10), 1091-9
CODEN: JFPRDR; ISSN: 0362-028X
PUBLISHER: International Association of Milk, Food and Environmental Sanitarians
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Outgrowth of proteolytic Clostridum **botulinum** type **A** and **B** spores in pasteurized process cheese products was assessed to acquire data for improved models of botulinum stability. High-moisture (58.5%) products were made with different levels of pH (5.45 to 5.9), **sodium chloride** (1.1 to 2.8%, wt/wt) and **citrates** or **phosphates** as emulsifying salts (1.5 to 2%, wt/wt), and held at 15 to 30°C. Supplemental expts. were carried out to address the effect of lactic acid concentration originating from the nonfat and 50% fat dry basis (FDB) cheese raw materials, of moisture (50 to 69%), and of total fat (0.1 to 41%, wt/wt). Colony counts were recorded as substitutes for the traditional times to toxin formation. In the last exptl. series a

polyclonal ELISA against type A and B toxin was carried out as an alternative to the mouse challenge test. Very low spore levels could lead to detectable toxin formation. **Temperature** strongly influenced outgrowth. At 18°C outgrowth only occurred in 3 mo at favorable aw (0.966) and pH (5.9). At 25°C, outgrowth occurred within one week under favorable conditions. No growth occurred within 3 mo when aw and pH were 0.95 and 5.55 resp. Polyphosphate appeared to be more inhibitory than **citrate**. Moisture is a frequently used indicator of botulinum stability, but when the FDB deviates from 50%, moisture is actually a poor indicator. Components such as **NaCl**, emulsifying salts, and lactic acid determine stability. Fat does not contribute to stability. Increased fat levels can reduce moisture without a concomitant increase in stability.

L36 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:679280 HCAPLUS
DOCUMENT NUMBER: 121:279280
TITLE: Inhibitory potential of four-carbon dicarboxylic acids on Clostridium botulinum spores in an uncured turkey product
AUTHOR(S): Miller, Arthur J.; Call, Jeffrey E.
CORPORATE SOURCE: Eastern Regional Research Center, Agricultural Research Service, Philadelphia, PA, 19118, USA
SOURCE: Journal of Food Protection (1994), 57(8), 679-83
CODEN: JFPRDR; ISSN: 0362-028X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Organic acids offer promising options for the food industry in its attempt to ensure product safety and to meet consumer demand for minimally processed foods. In this study, four-carbon dicarboxylic acids were individually screened for their inhibitory potential against proteolytic Clostridium botulinum spores. Ground turkey breast meat was formulated with 1.4% **sodium chloride** (**NaCl**), 0.3% sodium pyrophosphate, 2% organic acid, 8% water, and 500 spores/g of a six-strain mixture of proteolytic C. botulinum. Samples were adjusted to pH 6. Ten g of product in vacuum packages were heated in 75° water for 20 min, cooled, and incubated for 0 to 25 days at 28°. **Botulinal neurotoxin** was detected at two days in control samples (0% acid) and at five days in 2% malic acid (0.13 M), aspartic (0.13 M), tartaric (0.12 M), **succinic** (0.15 M), and fumaric (0.15 M) samples. Toxin was undetected at 25 days in samples treated with maleic acid (0.15 M). Maleic acid reduced total aerobic bacteria and lactic acid organisms in **temperature**-abused product, compared to controls. Further systematic investigation of these and related compds. with prior approval for food-use may demonstrate previously unrecognized antibacterial potential.

L36 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:598192 HCAPLUS
DOCUMENT NUMBER: 121:198192
TITLE: Peptide substrate specificity and properties of the zinc-endopeptidase activity of **botulinum** type **B neurotoxin**
AUTHOR(S): Shone, Clifford C.; Roberts, April K.
CORPORATE SOURCE: Protein Toxins Section, Cent. Appl. Microbiol. Res., Salisbury, SP4 0JG, UK

SOURCE: European Journal of Biochemistry (1994), 225(1), 263-70
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clostridium **botulinum** type **B neurotoxin** has been shown to be a zinc endopeptidase specific for vesicle-associated membrane protein (VAMP). A synthetic peptide of human/rat VAMP-2 [VAMP-2-(60-94)] is cleaved by the neurotoxin with the same specificity as that demonstrated for the membrane-associated protein (at the Gln76-Phe77 bond) and has been used to study the properties of the endopeptidase activity of the neurotoxin. Cleavage of the VAMP-2 peptide was demonstrated by both **botulinum** type **B neurotoxin** (Km = 3.3 + 10-4 M) and by its purified light subunit (Km = 3.5 + 10-4 M). The endopeptidase displayed a pH optimum of 7.0-7.5 and was inhibited by greater than 0.2 M **NaCl** and greater than 0.05 M sodium **phosphate**. Neurotoxin which had been inactivated by dialysis against EDTA could be re-activated by incubation with various divalent cations, notably Zn2+ and Cu2+. The substrate specificity of **botulinum** type **B neurotoxin** was studied using various analogs of VAMP-2 (60-94). The neurotoxin cleaved selectively to the N-terminal side of phenylalanine and tyrosine; no activity was observed with either leucine, valine or alanine in the P1' position. The properties of the P1 amino acid were less critical; the neurotoxin cleaving the C-terminus of glutamine, asparagine and alanine. A substrate analog with valine in the P1 position corresponding to the sequence of rat VAMP-1 was not cleaved. The rate of cleavage of a substrate analog representing the sequence of human VAMP-1, however, was more than twofold that of the VAMP-2 peptide. The properties and substrate specificity of **botulinum** type **B neurotoxin** suggest that the toxin represents a novel class of endopeptidase which requires a specific peptide substrate conformation for the expression of proteolytic activity.

L36 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:190022 HCAPLUS
DOCUMENT NUMBER: 120:190022
TITLE: Comparison of organic acid salts for Clostridium botulinum control in an uncured turkey product
AUTHOR(S): Miller, Arthur J.; Call, Jeffrey E.; Whiting, Richard C.
CORPORATE SOURCE: Eastern Reg. Res. Cent., Agric. Res. Serv., Philadelphia, PA, 19118, USA
SOURCE: Journal of Food Protection (1993), 56(11), 958-62
CODEN: JFPRDR; ISSN: 0362-028X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Health concerns have led consumers toward purchasing nitrite-free, low-salt meat and poultry products. Lacking these barriers to control growth of bacterial pathogens, such products carry heightened risks for botulism, especially if storage **temperature** is abused. To address this threat, 5 organic acid salts were evaluated as potential antibotulinal agents. Ground turkey breast was formulated with 1.4% **NaCl**, 0.3% sodium pyrophosphate, 0-6% organic acid salts, 10% ice, and 500 spores per g of a 6-strain mixture of proteolytic C. botulinum. Vacuum-packaged product (10 g) was heated in 75° water for 20 min, cooled, and incubated for up to 18 days at 28°. **Botulinal neurotoxin** was detected by

mouse bioassay at 2 days in samples which lacked any of the test compds. Samples containing 2% acid salt developed neurotoxin, which was detected at 2, 2, 4, 5, and 5 days for pyruvate, **citrate**, lactate, **acetate**, and propionate, resp. With 6% acid salt addns., samples remained neurotoxin free until 7 days with pyruvate, 18 days with **citrate**, and >18 days for the remaining compds. Monocarboxylic acid salts exhibited antibotulinal activity related to their dissociation consts. (pKa). **Citrate** did not fit this pattern, however, suggesting a different mechanism of action. This study reveals that a variety of organic acid salts possess activity that can be used alone or possibly in combination to enhance the safety of nitrite-free turkey products.

L36 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:630844 HCAPLUS
DOCUMENT NUMBER: 111:230844
TITLE: Sodium lactate delays **toxin** production by Clostridium **botulinum** in cook-in-bag turkey products
AUTHOR(S): Maas, M. R.; Glass, K. A.; Doyle, M. P.
CORPORATE SOURCE: Oscar Mayer Foods Corp., Madison, WI, 53707, USA
SOURCE: Applied and Environmental Microbiology (1989), 55(9), 2226-9
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Comminuted raw turkey, containing 1.4% **NaCl**, 0.3% Na **phosphate**, and 0 (control), 2.0, 2.5, 3.0, or 3.5% Na lactate, was inoculated with a 10-strain mixture of proteolytic type **A** and **B** C. **botulinum** spores. The inoculated turkey was vacuum packaged and cooked by immersion in heated water to an internal **temperature** of 71.1°. Samples were incubated at 27° for up to 10 days. Five samples per treatment were examined for **botulinal toxin** at specific intervals. Na lactate had a concentration-dependent antibotulinal effect. Processed turkey containing 0, 2.0, 2.5, 3.0, or 3.5% Na lactate was toxic after 3, 4-5, 4-6, 7, or 7-8 days, resp. Subsequent studies with a broth medium revealed that lactate, not Na+, was the principal factor in delaying toxin formation.

L36 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:109382 HCAPLUS
DOCUMENT NUMBER: 108:109382
TITLE: The combined effect of sub-optimal **temperature** and sub-optimal pH on growth and **toxin** formation from spores of Clostridium **botulinum**
AUTHOR(S): Graham, Ann F.; Lund, Barbara M.
CORPORATE SOURCE: Inst. Food Res., Norwich Lab., Norwich, NR4 7UA, UK
SOURCE: Journal of Applied Bacteriology (1987), 63(5), 387-93
CODEN: JABAA4; ISSN: 0021-8847
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Low-acid foods (pH ≥4.5) are not sufficiently acidic to prevent growth of C. botulinum in otherwise optimal conditions. The combination of sub-optimal pH and sub-optimal **temperature** may,

however, result in a very significant reduction in the risk of growth of this bacterium compared with the risk in optimal conditions. The combined effect of incubation **temps**. of 12° and 16° and pH values of 5.2-5.5 on growth and **toxin** production from spores of C. **botulinum** during incubation for 28 days was investigated. Growth and formation of toxin (type B) were detected only in medium at pH 5.5 and incubated at 16°, corresponding to a probability of growth from a single spore of 1.6 + 10-5 within **14** days. The probability of growth in 28 days was <9 + 10-6. After transfer of inoculated media from 12° to 30°, growth occurred within 19 days at pH 5.2-5.5. After transfer of inoculated media from 12° to 20°, growth occurred at pH 5.5 and 5.4 but not at pH 5.3 or 5.2 in 40 days. Growth at pH 5.2-5.5 was accompanied by formation of toxin, in most cases of types A or B. In addition to the effect of sub-optimal **temperature** and pH, chelation of divalent metals ions by **citrate** may have contributed to inhibition.

L36 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:456043 HCAPLUS
DOCUMENT NUMBER: 105:56043
TITLE: TLC immunostaining characterization of Clostridium **botulinum** type **A** **neurotoxin** binding to gangliosides and free fatty acids
AUTHOR(S): Takamizawa, Kotaro; Iwamori, Masao; Kozaki, Shunji; Sakaguchi, Genji; Tanaka, Ryuichiro; Takayama, Hiroo; Nagai, Yoshitaka
CORPORATE SOURCE: Fac. Med., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: FEBS Letters (1986), 201(2), 229-32
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The receptor structure of C. **botulinum** **neurotoxin** type **A** was analyzed by TLC immunostaining. Ganglioside GQ1b [68652-37-9] was the most potent receptor, and the neurotoxin also bound to ganglioside GT1b [59247-13-1] and ganglioside GD1a [12707-58-3], but not to ganglioside GM3 [54827-14-4], ganglioside GM2 [19600-01-2], ganglioside GM1 [37758-47-7], ganglioside GD3 [62010-37-1], ganglioside GD1b [19553-76-5], and ganglioside GT1a [64522-98-1]. Optimum binding of neurotoxin to the ganglioside appeared in 0.01M **phosphate buffer** (pH 7.2) containing 0.2% **NaCl**. Higher and lower **NaCl** concns. diminished neurotoxin binding to the ganglioside. In addition, the neurotoxin was able to bind to free fatty acids. Maximum binding was observed on stearic acid and neurotoxin binding to free fatty acids was not affected by **NaCl** concentration

L36 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:128561 HCAPLUS
DOCUMENT NUMBER: 104:128561
TITLE: Use of preservatives to delay **toxin** formation by Clostridium **botulinum** (type **B**, strain okra) in vacuum-packed, cooked potatoes
AUTHOR(S): Notermans, S.; Dufrenne, J.; Keybets, M. J. H.
CORPORATE SOURCE: Lab. Water Food Microbiol., Natl. Inst. Public Health Environ. Hyg., Bilthoven, 3720 BA, Neth.
SOURCE: Journal of Food Protection (1985), 48(10), 851-5

CODEN: JFPRDR; ISSN: 0362-028X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Storage at **temps**. below 4° prevents growth and **toxin** production by Closridium **botulinum** in vacuum-packed, cooked potatoes. The use of preservatives as an addnl., built-in safety factor has been investigated. Dipping potatoes in a solution of ascorbic [50-81-7] and citric acid [77-92-9] before vacuum-packing and cooking (95° for 50 min) inhibited growth and **toxin** production by proteolytic C. **botulinum** type **B** at an incubation **temperature** of 15° for 70 days and at 20° for ≥ **14** days. This preservative treatment also resulted in an organoleptically acceptable product with a prolonged shelf life. Risk anal. showed that the presence of C. botulinum in vacuum-packed, cooked potatoes may be expected, i.e., one spore in each 1585 kg of product. A preservative treatment with a combination of ascorbic and citric acid will limit the public health risk even if the potato product is accidentally stored for a short time at a **temperature** higher than 4°.

L36 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:128478 HCAPLUS
DOCUMENT NUMBER: 104:128478
TITLE: Plant trials of bacon made with lactic acid bacteria, sucrose and lowered sodium nitrite
AUTHOR(S): Tanaka, Nobumasa; Meske, Louise; Doyle, Michael P.; Traisman, Edwin; Thayer, Donald W.; Johnston, Ralph W.
CORPORATE SOURCE: Food Res. Inst., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Journal of Food Protection (1985), 48(8), 679-86
CODEN: JFPRDR; ISSN: 0362-028X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacon prepared with 40 and 80 mg/kg (ppm) $NaNO_2$, 0.7% sucrose [57-50-1], and a culture of Pediococcus acidilactici (Wisconsin Process), and control bacon prepared with 120 ppm $NaNO_2$ and no added sucrose or bacterial culture were produced at 3 com. bacon production plants. **NaCl**, **phosphate**, and Na ascorbate (or Na erythorbate) levels, as well as other processing conditions, such as pumping rate, smokehouse **temperature** and time, forming and slicing conditions, were those normally used by each plant. Randomly selected samples of each lot were used for a challenge experiment with Clostridium **botulinum** (types **A** and **B**), with .apprx.1000 heat-shocked spores/g bacon inoculated on each slice, vacuum packaged, and incubated at 27°. Samples were taken periodically up to 56 days of incubation and examined for the presence of **botulinal toxin**. Test bacon was substantially greater in antibotulinal properties than the control bacon. Residual $NaNO_2$ levels of test bacon were lower than those of the control bacon, as were nitrosamines formed upon frying. Average N-nitrosopyrrolidine [930-55-2] level was 8.6 μg/kg (ppb) in the control, <2.7 ppb in the 80-ppm NO_2^- product, and <1.6 ppb in the 40-ppm NO_2^- product. Thus, bacon com. prepared by the Wisconsin Process with 40 or 80 ppm $NaNO_2$ has a lesser risk of nitrosamine and **botulinal toxin** formation than bacon prepared with 120 ppm $NaNO_2$ and no added sucrose and lactic acid bacteria.

L36 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:547322 HCAPLUS
DOCUMENT NUMBER: 101:147322
TITLE: Simple and rapid method for extraction of proteins from bacteria
INVENTOR(S): Bhaduri, Saumya; Demchick, Paul H.
PATENT ASSIGNEE(S): United States Dept. of Agriculture, USA
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4464295	A	19840807	US 1983-524179	19830817
PRIORITY APPLN. INFO.:			US 1983-524179	19830817

AB Bacteria: Staphylococcus aureus, Escherichia coli, and Bacillus cereus were grown for 24 h in brain-heart infusion medium at 37°. Clostridium botulinum Was grown anaerobically in the same medium containing 1% arginine to delay autolysis. Cells from the cultures were harvested by centrifugation (7000 + g) washed twice with **phosphate buffered saline**, recentrifuged, resuspended in ice-cold acetone, allowed to stand for 5 min on ice, and collected by centrifugation. Residual acetone was removed and the protein were extracted by incubation with 1% SDS for 2 min. SDS-polyacrylamide gel electrophoresis indicated that the proteins obtained by the method was similar to that obtained by sonication or agitation with glass beads. The yield from S. aureus by acetone-SDS extraction was 200 mg protein/g dry weight of cells compared to 175 mg/g by the bead agitation technique. Yields for B. cereus, **E.** coli, and C. **botulinum** were 200, 225, and 150 mg proteins/g dry cell, resp. This method is inexpensive, rapid, simple and reproducible.

L36 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:42392 HCAPLUS
DOCUMENT NUMBER: 94:42392
TITLE: Isolation and properties of highly purified type **F** Clostridium **botulinum toxin**
AUTHOR(S): Uvarova, R. N.; Reshetnikova, L. N.; Ispolatovskaya, M. V.; Bulatova, T. I.
CORPORATE SOURCE: Inst. Epidemiol. Mikrobiol., Moscow, USSR
SOURCE: Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (1980), (11), 42-6
CODEN: ZMEIAV; ISSN: 0372-9311
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The steps involved in the isolation of C. **botulinum toxin** were initial precipitation with (NH4)2SO4 or Na hexametaphosphate after cultivation of the culture for 4 days at 28°, ultrafiltration through amicon membrane, gel filtration on 2 sephadex G-100 columns and elution with pH 5.6 Na **phosphate -phosphate buffer**, chromatog. on DEAE-cellulose, dialysis in a pH 4.2 **acetate buffer** containing 0.1 M **NaCl**, chromatog. on SP-sephadex (C-50), repeating of dialysis, ultrafiltration and then gel filtration on sephadex G-200, and finally

dialysis and chromatog. on DEAE-cellulose. The activity of the purified toxin ranged 1.5-4 + 107 (min. LD)/mg protein and had a mol. weight of 50,000 daltons.

L36 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:518322 HCAPLUS
DOCUMENT NUMBER: 91:118322
TITLE: Structure and toxicity of Clostridium **botulinum** type C **Toxin**
AUTHOR(S): Syuto, Bunei; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Japanese Journal of Medical Science & Biology (1979), 32(2), 132-3
CODEN: JJMCAQ; ISSN: 0021-5112
DOCUMENT TYPE: Journal
LANGUAGE: English
AB C. **botulinum Toxin** C could be separated into 2 peptide chains by chromatog. of QAE-Sephadex A-50 with a linear gradient of **NaCl** in 6% 2-mercaptoethanol-borate **phosphate buffer** at pH 8.1 and 0°. The components had different antigenicities and antitoxin to either chain neutralized the mother toxin toxicity. Combining the 2 chains gave an active form having 74% of the toxicity of the mother toxin; thus both chains are essential for toxicity. The reconstitution method affected the toxicity of the material prepared from the chains. Tryptophan and tyrosine residues were critical to maintain the toxin toxicity.

L36 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:169232 HCAPLUS
DOCUMENT NUMBER: 86:169232
TITLE: Effect of additional concentration and purification on the antigenic activity and chemical composition of toxoids for use in aerosol vaccines
AUTHOR(S): Shipulina, N. I.; Vasil'eva, I. P.; Didenko, L. A.; Shapareva, S. I.; Karpov, S. P.
CORPORATE SOURCE: Tomsk. Nauchno-Issled. Inst. Vaktsin Syvorotok, Tomsk, USSR
SOURCE: Trudy - Tomskii Nauchno-Issledovatel'skii Institut Vaktsin i Syvorotok, Tomskii Meditsinskii Institut [i] Tomskoe Otdelenie Vserossiiskogo Nauchno-Meditsinskogo Obshchestva Mikrobiologov, Epidemiologov i Parazitologov (1975), 25, 159-63
CODEN: TTVMA9; ISSN: 0130-4917
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The toxoids of Clostridium **botulinum** type **A**, **B**, and E were purified by precipitation at pH 3.3-3.5 and dialysis against **phosphate buffer** pH 6.81. C. tetani toxoids were precipitated with 15% **NaCl** and dialyzed against water. The content of Ca, Na, K, SO42-, B, P, and Cl decreased below those of starting crude toxoids. The antigenic activity and stability during storage also decreased after the purification

L36 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:400877 HCAPLUS
DOCUMENT NUMBER: 85:877
TITLE: Extraction and concentration of Clostridium

botulinum toxins from specimens
AUTHOR(S): Sonnenschein, B.; Bisping, W.
CORPORATE SOURCE: Inst. Mikrobiol. Tierseuchen, Tieraerztl. Hochsch. Hannover, Hannover, Fed. Rep. Ger.
SOURCE: Zentralblatt fuer Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Abteilung 1: Originale, Reihe A: Medizinische Mikrobiologie und Parasitologie (1976), 234(2), 247-59
CODEN: ZMMPAO; ISSN: 0300-9688
DOCUMENT TYPE: Journal
LANGUAGE: German
AB C. **botulinum toxins A-E** were added to canned green beans diluted 1:2 with 0.1M **phosphate buffer**, pH 6. The preparation was homogenized and centrifuged at 4000 rpm for 30 min. Fifteen ml of the supernatant was concentrated by Millipose ultrafiltration (membrane retaining material with mol. weight >25,000) to a volume of 0.5 ml. The 5 toxins were concentrated **14**.8-112.2-fold.

L36 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1974:105759 HCAPLUS
DOCUMENT NUMBER: 80:105759
TITLE: Germination of spores of Clostridium species capable of causing food poisoning. II. Effects of some chemicals on the germination of spores of C. **botulinum** type **A**
AUTHOR(S): Ando, Yoshiaki
CORPORATE SOURCE: Hokkaido Inst. Public Health, Sapporo, Japan
SOURCE: Shokuhin Eiseigaku Zasshi (1973), 14(5), 462-6
CODEN: SKEZAP; ISSN: 0015-6426
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Spores of C. **botulinum** type **A** 190 were heated at 70° for 10 min in 250mM **phosphate buffer** pH 6.7, cooled, and then incubated at 37° in germination medium containing 5mM L-alanine, 10mM Na L-lactate, 60mM NaHCO3, and 100mM **phosphate buffer** pH 6.7. Addition of 150mM D-alanine prevented germination. Addition of ≥5% **NaCl** or ≥1% Na sorbate to the medium retarded germination. EDTA, dipicolinic acid, and 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide showed no effect.

L36 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:85842 HCAPLUS
DOCUMENT NUMBER: 70:85842
TITLE: Purification and molecular dissociation of the precursor of Clostridium **botulinum** type **E toxin**
AUTHOR(S): Kitamura, Masaru; Sakaguchi, Simiko; Sakaguchi, Genji
CORPORATE SOURCE: Nat. Inst. Health, Tokyo, Japan
SOURCE: Anaerobic Bact., Proc. Int. Workshop, 5th (1968), Meeting Date 1967, 213-22. Editor(s): Fredette, V. Inst. Microbiol. Hyg. Montreal Univ.: Laval-des-Rapides, Can.
CODEN: 20QCAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The **toxin** of C. **botulinum** type **E** is

formed as a nontoxic ribonucleoprotein (I) which can be extracted from the cells with 0.2M **phosphate buffer**, pH 6.0. The protein moiety is purified by precipitation of I by half-saturated (NH4)2SO4, chromatog. on CM-Sephadex C-50 (II) at pH 6.0 (0.02M **acetate buffer**), digestion with RNase, rechromatog. on II at pH 6.0 with a linear concentration gradient of **NaCl** in 0.02M **acetate buffer**, precipitation by half-saturated (NH4)2SO4, chromatog. on Sephadex G-200, and rechromatog. on II. The toxicity of the product for mice was 2-8 LD50/mg. N, but activation by trypsin raised this to 5-10 LD50/mg. N. The material appeared homogeneous on disk electrophoresis (pH 4) and on ultracentrifugation (pH 4.5 or 6.0, s20, W 11.3-12.3 S), but gave 2 distinct precipitin lines on immunodiffusion and 2 distinct zones on electrophoresis (cellulose **acetate**) at pH 7. Ultracentrifugation at pH 8 (0.05M Veronal **buffer**) gave a single major band, s20, W 7.3 S. Starch-gel electrophoresis at pH 8 (0.05M Veronal **buffer**) gave partial separation into anodic and cathodic peaks; only the latter gave active toxin after treatment with trypsin.

L36 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:46431 HCAPLUS
DOCUMENT NUMBER: 68:46431
TITLE: Chromatographic isolation of hemagglutinin-free **neurotoxin** from crystalline **toxin** of Clostridium **botulinum** type **A**
AUTHOR(S): DasGupta, Bibhuti R.; Boroff, Daniel A.
CORPORATE SOURCE: Albert Einstein Med. Center, Philadelphia, PA, USA
SOURCE: Biochimica et Biophysica Acta, Protein Structure (1967), 147(3), 603-5
CODEN: BBPTBH; ISSN: 0005-2795
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Crystalline toxin in 0.025 M **phosphate** (I) **buffer** was applied to a DEAE-cellulose column equilibrated with the **buffer**, and eluted with a linear gradient of I. Three distinct peaks plus a trace 4th peak were eluted. The 1st (**14** .6% of the total eluted protein) was highly toxic, and showed no hemagglutinating activity. The next 2 strongly agglutinated red blood cells. The 1st peak was the α fraction previously obtained with Tris-HCl **buffer** chromatog. (loc. cit.). It was possible to sep. the α fraction by a 2nd, simpler procedure employing I **buffer**, without application of a gradient elution. The purification on DEAE-cellulose appeared to be as good with I as with Tris-HCl **buffer**. Isolation of the hemagglutinin-free neurotoxin by elution with 0.05M gave higher yields of this fraction than did elution with 0.025M I or Tris-HCl **buffer**. Substitution of Cl- with I did not appear to alter the resolution pattern of crystalline toxin or the neurotoxin. The fraction showed chromatog. homogeneity in both I and Tris-HCl **buffer**.

L36 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:20941 HCAPLUS
DOCUMENT NUMBER: 68:20941
TITLE: Demonstration of bacterial toxins in foodstuffs by means of immunofluorescence
AUTHOR(S): Riemann, Hans
CORPORATE SOURCE: Sch. of Vet. Med., Univ. of California, Davis, CA, USA

SOURCE: Nordisk Veterinaermedicin (1967), 19(4), 188-94
CODEN: NOVTAV; ISSN: 0029-1579
DOCUMENT TYPE: Journal
LANGUAGE: Danish

AB Staphylococcal enterotoxin B antitoxin, obtained from rabbits, was conjugated with fluorescein isothiocyanate and purified on DEAE-cellulose and Sephadex columns. The conjugate was adsorbed to nontoxin-producing staphylococcal strains and purified as Sephadex. To avoid false neg. results due to extracellular localization of toxin, the conjugate and culture, after incubation at 30° for 30 min. and at 20° for 4 hrs., were filtered through a 0.22-μ pore filter plus Whatman Number 1 filter paper. Direct preparates were prepared by growing cultures on dialysis membranes mounted on blood-agar. The preparate was freeze-dried and colored by incubation with conjugate at 37°. With these methods 1 γ toxin/ml. sample was detected. In a quant. modification, antiserum and agar were mixed (50:50) and poured into small glass tubes. Test solution was pipetted on the gel and after 1-7 days incubation, the amount of toxin was estimated, being related to the distance between the surface and the line of precipitation With this method 4 γ/ml. were detectable after 8 days and 8 γ/ml. after 1 day. The toxin was identified by gel-diffusion technique. These methods were used for determination of toxin in various foods. It was found that 1-10 γ toxin was formed per g. ham on anaerobic storage for 8-13 days at room **temperature** The amount of toxin formed varied according to pH and salt concentration At pH 6.9 and **NaCl** concentration 10-12 g./100 ml. and pH 5.1 and **NaCl** concentration 4 g./100 ml. both totally inhibited production of toxin. Com. Clostridium **botulinum E** antiserum was purified by precipitation with (NH4)2SO4 and chromate on Sephadex and in two steps adsorbed to nontoxin-producing and **toxin**-producing C. **botulinum E.** Com. rabbit antihorse serum γ-globulin, conjugated with fluorescein isothiocyanate was dialyzed against a **phosphate buffer** and chromatographed on a DEAE-cellulose column. Preparates were incubated with antitoxin for 0.5-1 hr. at 37° and again under the same conditions with rabbit antihorse serum. Neither nontoxic strain E nor strain A or B or pseudobotulinum E from toxic cultures of strain E showed fluorescence with reagent. Toxic cultures of strain E showed no fluorescence when tested against antitoxin A or B. Incubations of ham showed, when tested on mice, that toxin was produced when the salt concentration decreased under 2.5 g./100 ml. H_2O; these expts., however, were neg. to the fluorescence being described.

L36 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:45110 HCAPLUS
DOCUMENT NUMBER: 56:45110
ORIGINAL REFERENCE NO.: 56:8479f-h
TITLE: Decontamination of drinking water with mobile equipment
AUTHOR(S): Mehls, Karl F. H.
SOURCE: GWF, das Gas- und Wasserfach (1961), 102, 1365-9
CODEN: GAWFAN; ISSN: 0367-3839
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB This is an abridgment of an article to be published as a Dechema monograph. A discussion is presented of the field use of mobile equipment to remove radioactivity, bacteria, viruses, botulins, and war gases from drinking water. In general, better results are secured

by adding filter material, reagents, etc., to the water than by using fixed filter beds. Kieselguhr can be treated with Ag to have a bactericidal effect. Cl kills bacteria and viruses and destroys biol. warfare materials such as the **botulinus toxins** in **a** few min. This is most conveniently supplied as NaClO from the electrolysis of **NaCl** solns., although Ca(ClO)2 can also be used. Where war gases such as **phosphate** esters, are present, these can be removed by hydrolysis at a high pH in the presence of hypochlorite. Adsorption followed by precipitation and the use of flocculants is also suggested. Radioactivity can readily be removed by mixed-bed deionization filters, but the mixed-bed resin deteriorates with time, especially when stored at elevated **temps**. Handling of the contaminated resin and regeneration is also a problem. M. uses a cation exchanger operating on a Na cycle. Patent coverage on decontamination processes is cited.

L36 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:90076 HCAPLUS
DOCUMENT NUMBER: 50:90076
ORIGINAL REFERENCE NO.: 50:16971f-h
TITLE: Isolation of an aminopeptidase from type **B** Clostridium **botulinum**
AUTHOR(S): Millonig, Robert C.
CORPORATE SOURCE: Johns Hopkins Univ., Baltimore, MD
SOURCE: Journal of Bacteriology (1956), 72, 301-7
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A method is described for the purification of a proteinase in the culture supernatant of type **B** C. **botulinum** (Okra strain) by fractional precipitation with (NH4)2SO4 and subsequent repptn. with **NaCl** under controlled conditions of pH, (NH4)2SO4 concentration, and **temperature** The method is rapid and permits purification of approx. 300-fold with a 15% loss in the amount of enzyme recovered. Solubility measurements and ultracentrifuge analysis on the purified prepns. indicate the presence of one component. The proteinase was found to contain little or no tyrosine and tryptophan by study of its absorption in the ultraviolet spectrum. The purified product appears to contain but one proteinase which is optimally activated by Fe++-cysteine; and was shown to be an aminopolypeptidase capable of splitting tripeptides but not dipeptides. The ferrous ion is necessary for activity of the enzyme. Binding the ferrous ion with Versene renders the proteinase inactive.

L36 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1947:6248 HCAPLUS
DOCUMENT NUMBER: 41:6248
ORIGINAL REFERENCE NO.: 41:1275c-e
TITLE: Molecular weight and homogeneity of crystalline **botulinus A toxin**
AUTHOR(S): Putnam, Frank W.; Lamanna, Carl; Sharp, D. G.
CORPORATE SOURCE: Camp Detrick, Frederick, MD
SOURCE: Journal of Biological Chemistry (1946), 165, 735-6
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 40, 4767.2, 6121.2. The electrophoretic, sedimentation, and

diffusion characteristics of crystalline Clostridium **botulinum** type **A toxin** have been studied in 0.1 N Na **acetate buffer,** pH 4.38. The toxin is electrophoretically homogeneous and has a mobility of 2.75 + 10-5 sq. cm. volt-1 sec.-1. The ultracentrifugal sedimentation diagrams show a single symmetrical boundary and yield a value of S20 = 17.3 Svedberg units. The diffusion constant of a 0.63% solution at 25° by the refractometric scale method is 2.**14** + 10-7 sq. cm. sec.-1. Satisfactory agreement at successive time intervals among the values calculated by different methods and a good fit of the normalized diffusion curves with the ideal distribution curve have been realized. The boundary spread in the ultracentrifuge is greater than that attributable to diffusion alone. If a partial sp. volume of 0.75 is assumed, the mol. weight calculated from S20 and D20 is 900,000 (cf. C.A. 40, 6560.1); this suggests the presence of 2.1 + 107 mols. per mouse LD50. A tentative frictional value of 1.76 is assigned. If the mols. are assumed to be prolate elipsoids, this figure corresponds to an axial ratio, b/a = **14**.6, neglecting hydration.

L36 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1924:26723 HCAPLUS
DOCUMENT NUMBER: 18:26723
ORIGINAL REFERENCE NO.: 18:3621g-i
TITLE: Optimum and limiting hydrogen-ion concentrations for **B. botulinus** and quantitative estimation of its growth. XVI
AUTHOR(S): Dozier, Carrie C.
SOURCE: Journal of Infectious Diseases (1924), 35, 105-33
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The optimum range of H-ion concentration for **B. botulinus** in **phosphate-buffered** double-strength veal infusion + 2% Difco peptone is pH 6.0 to 8.2, inclusive, with a mean near pH 7.0, when vegetative forms are planted. The limiting range for 3-day growths is from pH 5 to 9, inclusive. The indications are that a slight acidity may be a stimulus to spore germination. Approx. the same optimum zone, pH 6.0 to 8.9. was demonstrated for **B**. **botulinus, B.** sporogenes and **B.** histolyticus vegetative inoculums in autolyzed veal infusion. **B. botulinus** grows well at 37°, but the number of viable organisms decreased rapidly at such a **temperature** The peak of proliferation is reached somewhat more slowly at 26.5°, and the decline in nos. is retarded. The decline in nos. is followed by autolysis, which is probably the mechanism of toxin formation. Vegetable mediums support fair growth of **B**. **botulinus.** The most active limiting factor in such mediums seems to be the natural acidity.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 12:02:38 ON 27 OCT 2005)

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON BOTOX/CN
L2 6 SEA FILE=REGISTRY ABB=ON PLU=ON BOTULIN TOXIN? /CN
L3 8 SEA FILE=REGISTRY ABB=ON PLU=ON BOTULIN NEUROTOXIN? /CN
L4 8 SEA FILE=REGISTRY ABB=ON PLU=ON BOTULINUM TOXIN? /CN
L5 14 SEA FILE=REGISTRY ABB=ON PLU=ON BOTULINUM NEUROTOXIN?

```
                /CN
L6          134 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN A ? OR BOTULIN
                B ? OR BOTULIN C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR
                BOTULIN E ? OR BOTULIN F ?)/CN
L7            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULINUM A ? OR
                BOTULINUM B ? OR BOTULINUM C1 ? OR BOTULINUM C2 ? OR
                BOTULINUM D ? OR BOTULINUM E ? OR BOTULINUM F ?)/CN
L8          156 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR
                L5 OR L6 OR L7
L9            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (PHOSPHATE/CN OR
                "PHOSPHATE (32PO4)"/CN OR "PHOSPHATE (H2PO4-)"/CN OR
                "PHOSPHATE (H2PO41-)"/CN OR "PHOSPHATE (HPO42-)"/CN OR
                "PHOSPHATE (P2O74-)"/CN OR "PHOSPHATE (P4O123-)"/CN) OR
                "PHOSPHATE (P6O186-)"/CN OR ("PHOSPHATE (PO3-)"/CN OR
                "PHOSPHATE (PO31-)"/CN OR "PHOSPHATE (PO32-)"/CN) OR
                "PHOSPHATE (PO43-)"/CN OR "PHOSPHATE (PO4H2-)"/CN
L10           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CITRATE/CN
L11           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACETATE/CN
L12           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SUCCINATE/CN
L13          12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 OR L10 OR L11 OR L12
L15           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN G ? OR BOTULINUM
                 G ?)/CN
L16         161 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L15
L18     1354347 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR PHOSPHATE OR
                CITRATE OR ACETATE OR SUCCINATE OR SUCCINIC OR BUTANEDIOIC
                OR ACETIC
L27        6302 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR (BO OR BOTULIN?)(5A
                )(NT OR TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR
                BOTX# OR BTX# OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(
                3A)(A OR B OR C1 OR C2 OR D OR E OR F OR G)
L28         290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND L18
L29          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND (14 OR NACL OR
                (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALINE)
L34          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND BUFFER?
L37          63 SEA L34
L39          35 SEA L37 AND (PH OR (H OR HYDROGEN)(W) ION)


L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTOX/CN
L2            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULIN TOXIN? /CN
L3            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULIN NEUROTOXIN? /CN
L4            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULINUM TOXIN? /CN
L5           14 SEA FILE=REGISTRY ABB=ON  PLU=ON  BOTULINUM NEUROTOXIN?
                /CN
L6          134 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN A ? OR BOTULIN
                B ? OR BOTULIN C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR
                BOTULIN E ? OR BOTULIN F ?)/CN
L7            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULINUM A ? OR
                BOTULINUM B ? OR BOTULINUM C1 ? OR BOTULINUM C2 ? OR
                BOTULINUM D ? OR BOTULINUM E ? OR BOTULINUM F ?)/CN
L8          156 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR
                L5 OR L6 OR L7
L9            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (PHOSPHATE/CN OR
                "PHOSPHATE (32PO4)"/CN OR "PHOSPHATE (H2PO4-)"/CN OR
                "PHOSPHATE (H2PO41-)"/CN OR "PHOSPHATE (HPO42-)"/CN OR
                "PHOSPHATE (P2O74-)"/CN OR "PHOSPHATE (P4O123-)"/CN) OR
                "PHOSPHATE (P6O186-)"/CN OR ("PHOSPHATE (PO3-)"/CN OR
                "PHOSPHATE (PO31-)"/CN OR "PHOSPHATE (PO32-)"/CN) OR
                "PHOSPHATE (PO43-)"/CN OR "PHOSPHATE (PO4H2-)"/CN
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see L58-L65

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L10           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CITRATE/CN
L11           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACETATE/CN
L12           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SUCCINATE/CN
L13          12 SEA FILE=REGISTRY ABB=ON  PLU=ON  L9 OR L10 OR L11 OR L12
L15           6 SEA FILE=REGISTRY ABB=ON  PLU=ON  (BOTULIN G ? OR BOTULINUM
                  G ?)/CN
L16         161 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L15
L18     1354347 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 OR PHOSPHATE OR
                  CITRATE OR ACETATE OR SUCCINATE OR SUCCINIC OR BUTANEDIOIC
                  OR ACETIC
L27        6302 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR (BO OR BOTULIN?)(5A
                  )(NT OR TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR
                  BOTX# OR BTX# OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(
                  3A)(A OR B OR C1 OR C2 OR D OR E OR F OR G)
L28         290 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND L18
L29          66 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 AND (14 OR NACL OR
                  (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALINE)
L35          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND (TEMP OR TEMPERATU
                  RE)
L38          46 SEA L35
L43           9 SEA L38 AND (STORE# OR STORING OR STORAGE)


L44          39 S (L39 OR L43) NOT L32
L45          20 DUP REM L44 (19 DUPLICATES REMOVED)
```

L45 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005010262 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15635936
TITLE: Factors affecting autocatalysis of **botulinum A neurotoxin** light chain.
AUTHOR: Ahmed S Ashraf; Ludivico Matthew L; Smith Leonard A
CORPORATE SOURCE: Department of Immunology and Molecular Biology, Division of Toxinology and Aerobiology, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD 21702, USA.. syed.ahmed@amedd.army.mil
SOURCE: Protein J, (2004 Oct) 23 (7) 445-51.
Journal code: 101212092. ISSN: 1572-3887.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20050108
Last Updated on STN: 20050415
Entered Medline: 20050414

AB The light chain of **botulinum neurotoxin** serotype **A** undergoes autocatalytic fragmentation into two major peptides during purification and storage (Ahmed S. A. et al. 2001, J. Protein Chemical 20:221-231) by both intermolecular and intramolecular mechanisms (Ahmed S. A. et al. 2003, Biochemistry 42:12539 12549). In this study, we investigated the effects of **buffers** and salts on this autocatalytic reaction in the presence and absence of zinc chloride. In the presence of zinc chloride, the fragmentation reaction was enhanced in each of **acetate**, MES, HEPES and **phosphate buffers** with maximum occurring in **acetate** when compared to those in the absence of zinc chloride. Adding **sodium chloride** in **phosphate buffer** in the presence of zinc chloride

increased the extent of proteolysis. Irrespective of the presence of zinc chloride, adding **sodium chloride** or potassium chloride in **phosphate buffer** elicited an additional proteolytic reaction. Higher concentrations of sodium **phosphate buffer** enhanced the autocatalytic reaction in the absence of zinc chloride. In contrast, in the presence of zinc chloride, higher concentrations of sodium **phosphate** decreased the autocatalytic reaction. Optimum **pH** of autocatalysis was not affected significantly by the absence or presence of zinc chloride. Like zinc chloride, other chlorides of divalent metals, such as magnesium, cobalt, iron and calcium also enhanced the autocatalytic reaction. Polyols such as ethylene glycol protected the light chain from fragmentation. Exposure of light chain to UV radiation led to enhanced fragmentation. In order to avoid fragmentation, the protein should be stored frozen in a low concentration **buffer** of neutral or higher **pH** devoid of any metal. Our results provide a choice of **buffers** and salts for isolation, purification and storage of intact **botulinum neurotoxin** serotype **A** light chain.

L45 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2003544311 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14623391
TITLE: Combined effects of ionizing-irradiation and different environments on Clostridium **botulinum** type **E** spores.
AUTHOR: Lim Y H; Hamdy M K; Toledo R T
CORPORATE SOURCE: Department of Food Science and Technology, University of Georgia, Athens, GA 30602, USA.
SOURCE: International journal of food microbiology, (2003 Dec 31) 89 (2-3) 251-63.
Journal code: 8412849. ISSN: 0168-1605.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040213
Entered Medline: 20040212

AB We examined the combined effects of gamma-radiation (24 degrees C) on spores of Clostridium botulinum-type Eklund strain suspended in different gas-saturated Na-**phosphate buffer** in absence or presence of protectors or sensitizers. Response surface methodology (RSM) was also used to ascertain the effects of radiation on the recovery of spores using a medium containing various levels of **NaCl** or Na-thioglycollate. The former (< 0.5%) decreased viable spore counts, but the latter (0.15%) did not. Irradiation inactivation of Eklund spores was most effective in air-saturated **buffers** compared to N2O and N2 gas. The Na2-EDTA (0.01 M) was the most efficient radioprotector of spores due to its reactivity toward hydroxy radicals, followed by t-butanol (0.1 M) in NO2 or N(2)-saturated **buffers**, respectively. Catalase (10.0 mg ml(-1)) and DL-cysteine (0.1 mM) sensitized the spores during irradiated N2O or N(2)-saturated **buffers**, and **NaCl** (0.01 M) only sensitized spores in N2 environment. Spores frozen at -75 degrees C for 30 days and thawed prior to use were more sensitive to radiation damage compared to freshly prepared spores. Glycerol

(15%), in Na-**phosphate buffer** (**pH** 7.0, 0.06 M), protected Eklund spores and increased the number of spores from 10(6) to 10(11) colony forming unit (CFU) ml(-1), and enhanced their radiosensitivities. Seven strains of C. **botulinum** type **E** were screened for plasmids and strain BL764 had two plasmids (15.8 and 46.8 mDa), BL4028 also had two (4.4 and 13.2 mDa), BL4850 contained only one (4.9 mDa), whereas EQA, BL211, Eklund, and Beluga had none. Gamma-Radiation (10 kGy, absorbed dose) cured the 15.8-mDa plasmid in strain BL764, but its absence yielded no changes in toxigenicity.

L45 ANSWER 3 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-049992 [06] WPIDS
DOC. NO. CPI: C2001-013779
TITLE: Composition useful for e.g. treating nervous system disorders, comprising **botulinum neurotoxin**, is free from natural complexing proteins and is not antigenic.
DERWENT CLASS: B04 D16
INVENTOR(S): BIGALKE, H; FREVERT, J
PATENT ASSIGNEE(S): (BIOT-N) BIOTECON-GES BIOTECHNOLOGISCHE; (MERZ-N) MERZ PHARMA GMBH & CO KGAA; (MRZC) MERZ & CO GMBH & CO; (MRZC) MERZ PHARMA GMBH & CO KGAA; (MRZC) MERZ PHARMA GMBH & CO KG
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000074703	A2	20001214	(200106)*	GE	14
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
DE 19925739	A1	20001221	(200106)		
AU 2000058047	A	20001228	(200119)		
DE 10081516	T	20010913	(200153)		
NO 2001005964	A	20020130	(200223)		
EP 1185291	A2	20020313	(200225)	GE	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CZ 2001004351	A3	20020612	(200251)		
KR 2002008214	A	20020129	(200253)		
CN 1354670	A	20020619	(200263)		
HU 2002001530	A2	20020930	(200272)		
JP 2003505343	W	20030212	(200321)		27
ZA 2001010074	A	20030528	(200341)		36
EP 1185291	B1	20040204	(200410)	GE	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
DE 50005208	G	20040311	(200425)		
ES 2215056	T3	20041001	(200466)		
AU 774590	B2	20040701	(200469)		
KR 466407	B	20050127	(200535)		
MX 2001012540	A1	20041101	(200558)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000074703	A2	WO 2000-DE1777	20000526
DE 19925739	A1	DE 1999-1025739	19990607
AU 2000058047	A	AU 2000-58047	20000526
DE 10081516	T	DE 2000-10081516	20000526
		WO 2000-DE1777	20000526
NO 2001005964	A	WO 2000-DE1777	20000526
		NO 2001-5964	20011206
EP 1185291	A2	EP 2000-943666	20000526
		WO 2000-DE1777	20000526
CZ 2001004351	A3	WO 2000-DE1777	20000526
		CZ 2001-4351	20000526
KR 2002008214	A	KR 2001-715668	20011205
CN 1354670	A	CN 2000-808641	20000526
HU 2002001530	A2	WO 2000-DE1777	20000526
		HU 2002-1530	20000526
JP 2003505343	W	WO 2000-DE1777	20000526
		JP 2001-501237	20000526
ZA 2001010074	A	ZA 2001-10074	20011206
EP 1185291	B1	EP 2000-943666	20000526
		WO 2000-DE1777	20000526
DE 50005208	G	DE 2000-00005208	20000526
		EP 2000-943666	20000526
		WO 2000-DE1777	20000526
ES 2215056	T3	EP 2000-943666	20000526
AU 774590	B2	AU 2000-58047	20000526
KR 466407	B	WO 2000-DE1777	20000526
		KR 2001-715668	20011205
MX 2001012540	A1	WO 2000-DE1777	20000526
		MX 2001-12540	20011205

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000058047	A	Based on	WO 2000074703
DE 10081516	T	Based on	WO 2000074703
EP 1185291	A2	Based on	WO 2000074703
CZ 2001004351	A3	Based on	WO 2000074703
HU 2002001530	A2	Based on	WO 2000074703
JP 2003505343	W	Based on	WO 2000074703
EP 1185291	B1	Based on	WO 2000074703
DE 50005208	G	Based on	EP 1185291
		Based on	WO 2000074703
ES 2215056	T3	Based on	EP 1185291
AU 774590	B2	Previous Publ.	AU 2000058047
		Based on	WO 2000074703
KR 466407	B	Previous Publ.	KR 2002008214
		Based on	WO 2000074703
MX 2001012540	A1	Based on	WO 2000074703

PRIORITY APPLN. INFO: DE 1999-19925739 19990607
AN 2001-049992 [06] WPIDS
AB WO 200074703 A UPAB: 20041015
NOVELTY - Pharmaceutical composition containing one or more **botulinum neurotoxins** (A) from Clostridium **botulinum** types **A-G** in which (A) is free

Searcher : Shears 571-272-2528

of proteins that are naturally combined with (A) in complexes, is new.

ACTIVITY - Antispasmodic; antimigraine. A patient, with torticollis spasmodicus had been treated with **Botox** (RTM for native neurotoxin-protein complexes) for 5 years and produced neutralizing antibodies, so no longer responded to treatment. He was treated with 145 units of uncomplexed (A), equivalent to the doses of **Botox** (RTM) previously given, and within 72 hr the muscles were relaxed, the head was held normally and muscular pain was alleviated. No adverse effects were observed.

MECHANISM OF ACTION - Motor end plate nerve ending binder.

USE - The composition is used:

(i) to treat nervous system disorders and dystonia (specifically torticollis spasmodicus, belpherospasm, spasticity, hemifacial spasm, migraine, lumbalgia, cervical syndrome and hypersalivation); and

(ii) cosmetically to treat hyperhidrosis and facial wrinkles, most particularly in subjects who already produce neutralizing antibodies against the native complexes.

ADVANTAGE - (A) induces neutralizing antibodies to a lesser extent than the native complexes, or not at all, so can be used for long term treatment. Also it is available immediately and binds directly to nerve endings on the motor end plate. Rats were intracutaneously injected with native (A)-protein complexes or free (A), at 200 pg (A). Four of 8 animals treated with the complex developed neutralizing antibodies that inhibited activity of the toxin, but none of those treated with uncomplexed (A) did.

Dwg.0/0

L45 ANSWER 4 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2001:123675 TOXCENTER
COPYRIGHT:	Copyright 2005 ACS
DOCUMENT NUMBER:	CA13504043124S
TITLE:	Method of immunoenzymic detection of **botulin toxin** and apparatus for the detection
AUTHOR(S):	Trojan, Czeslaw; Kuczek, Marian
CORPORATE SOURCE:	ASSIGNEE: Wyzsza Szkola Oficerska im.Tadeusza Kosciuszki
PATENT INFORMATION:	PL 179790 B1 31 Oct 2000
SOURCE:	(2000) Pol., 4 pp. CODEN: POXXA7.
COUNTRY:	POLAND
DOCUMENT TYPE:	Patent
FILE SEGMENT:	CAPLUS
OTHER SOURCE:	CAPLUS 2001:491426
LANGUAGE:	Polish
ENTRY DATE:	Entered STN: 20011116 Last Updated on STN: 20020319

AB A semiquant. field method for the immunoenzymic detection of **botulin toxin** on glass fiber paper Whatman GF/A is described. Anti-botulotoxin antibodies labeled with fluorescein isothiocyanate (FITC) are fixed on the dry paper in a vertical line. The crossing horizontal line made under UV lamp contains similarly FITC-labeled antibodies with **botulin toxin** or toxoid. After drying the paper is saturated with 1% casein. On the prepared paper, a drop of the aqueous extract of the sample is applied, followed by 0.5 mL stabilized anti-botulotoxin antibodies labeled with peroxidase (1 μg/mL in 0.1 M **phosphate buffer** **pH** 6.5). After soaking of the solns. into the paper and drying, the paper surface is washed with 1% aqueous **NaCl** with 0.01% cetylpyrimidine HCl detergent in 0.01% **phosphate**

buffer pH 6.5. Subsequently a drop of alc. solution of the chromogenic substrate (tetramethylbenzidine chloride or sulfate) and H2O2 are added. The developed color is visually judged pos. or neg. for the **botulin toxin** presence it the sample examined A simple box device for the test execution is described.

L45 ANSWER 5 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:197733 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12721292350T
TITLE: Low-acid, high-moisture processed cheese spread and method of making
AUTHOR(S): Adrianson, Tim M.; Brown, Alpheus I., Jr.; Busk, G. Curtis, Jr.; Gunther, Stephen A.; Huether, Karen D.; Mann, Joseph W.; Yoss, James K.
CORPORATE SOURCE: ASSIGNEE: Nabisco, Inc.
PATENT INFORMATION: US 5670197 A 23 Sep 1997
SOURCE: (1997) U.S., 11 pp.
CODEN: USXXAM.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1997:636107
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020618

AB High-moisture, high-pH, shelf-stable cheese spreads containing cheese, preferably a cheese having a pH of 5.4 or lower such as Swiss, Cheddar, American, mozzarella, skim milk cheese, or cheese mixts., water sufficient to provide a total moisture of from 51 to 58% and a pH of from 5.3 to 6.0 are preserved by adding **sodium chloride**, a **phosphate** salt, sodium **citrate** , and sodium lactate in sufficient amts. to maintain the composition free from the growth of Clostridium **botulinum** and the production of **toxin** by those organisms during room **temperature storage** for a period of at least 180 days, preferably 300 days. Some embodiments contain 1 to 2% sodium **citrate**, 1 to 2% sodium lactate, and a combined level of dibasic sodium **phosphate** and **sodium chloride** ranging between 1.3 and 2.2%, and have a moisture content of 52 to 55%, and an overall pH of about 5.3 to 5.6.

L45 ANSWER 6 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:135065 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12015190022A
TITLE: Comparison of organic acid salts for Clostridium botulinum control in an uncured turkey product
AUTHOR(S): Miller, Arthur J.; Call, Jeffrey E.; Whiting, Richard C.
CORPORATE SOURCE: Eastern Reg. Res. Cent., Agric. Res. Serv., Philadelphia, PA, 19118, USA.
SOURCE: Journal of Food Protection, (1993) Vol. 56, No. 11, pp. 958-62.
CODEN: JFPRDR. ISSN: 0362-028X.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1994:190022

LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020917

AB Health concerns have led consumers toward purchasing nitrite-free, low-salt meat and poultry products. Lacking these barriers to control growth of bacterial pathogens, such products carry heightened risks for botulism, especially if **storage temperature** is abused. To address this threat, 5 organic acid salts were evaluated as potential antibotulinal agents. Ground turkey breast was formulated with 1.4% **NaCl**, 0.3% sodium pyrophosphate, 0-6% organic acid salts, 10% ice, and 500 spores per g of a 6-strain mixture of proteolytic C. botulinum. Vacuum-packaged product (10 g) was heated in 75° water for 20 min, cooled, and incubated for up to 18 days at 28°. **Botulinal neurotoxin** was detected by mouse bioassay at 2 days in samples which lacked any of the test compds. Samples containing 2% acid salt developed neurotoxin, which was detected at 2, 2, 4, 5, and 5 days for pyruvate, **citrate**, lactate, **acetate**, and propionate, resp. With 6% acid salt addns., samples remained neurotoxin free until 7 days with pyruvate, 18 days with **citrate**, and >18 days for the remaining compds. Monocarboxylic acid salts exhibited antibotulinal activity related to their dissociation consts. (pKa). **Citrate** did not fit this pattern, however, suggesting a different mechanism of action. This study reveals that a variety of organic acid salts possess activity that can be used alone or possibly in combination to enhance the safety of nitrite-free turkey products.

L45 ANSWER 7 OF 20 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 86220811 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3709810
TITLE: TLC immunostaining characterization of Clostridium **botulinum** type **A neurotoxin** binding to gangliosides and free fatty acids.
AUTHOR: Takamizawa K; Iwamori M; Kozaki S; Sakaguchi G; Tanaka R; Takayama H; Nagai Y
SOURCE: FEBS letters, (1986 Jun 9) 201 (2) 229-32.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860714

AB The receptor structure of Clostridium **botulinum neurotoxin** type **A** was analysed by TLC immunostaining. GQ1b was found to be the most potent receptor, and the neurotoxin also bound to GT1b and GD1a, but not to GM3, GM2, GM1, GD3, GD1b and GT1a. Optimum binding of neurotoxin to the ganglioside appeared in 0.01 M **phosphate buffer** (**pH** 7.2) containing 0.2% **NaCl**. Higher and lower **NaCl** concentrations diminished neurotoxin binding to the ganglioside. In addition, the neurotoxin was able to bind to free fatty acids. Maximum binding was observed on stearic acid and neurotoxin binding to free fatty acids was not affected by **NaCl** concentration.

L45 ANSWER 8 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:118339 TOXCENTER

DOCUMENT NUMBER: CA104151285615
TITLE: Use of preservatives to delay **toxin** formation by Clostridium **botulinum** (type **B**, strain okra) in vacuum-packed, cooked potatoes
AUTHOR(S): Notermans, S.; Dufrenne, J.; Keybets, M. J. H.
CORPORATE SOURCE: Lab. Water Food Microbiol., Natl. Inst. Public Health Environ. Hyg., Bilthoven, 3720 BA, Neth..
SOURCE: Journal of Food Protection, (1985) Vol. 48, No. 10, pp. 851-5.
CODEN: JFPRDR. ISSN: 0362-028X.
COUNTRY: NETHERLANDS
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1986:128561
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20050517

AB **Storage** at **temps**. below 4° prevents growth and **toxin** production by Closridium **botulinum** in vacuum-packed, cooked potatoes. The use of preservatives as an addnl., built-in safety factor has been investigated. Dipping potatoes in a solution of ascorbic [50-81-7] and citric acid [77-92-9] before vacuum-packing and cooking (95° for 50 min) inhibited growth and **toxin** production by proteolytic C. **botulinum** type **B** at an incubation **temperature** of 15° for 70 days and at 20° for ≥ **14** days. This preservative treatment also resulted in an organoleptically acceptable product with a prolonged shelf life. Risk anal. showed that the presence of C. botulinum in vacuum-packed, cooked potatoes may be expected, i.e., one spore in each 1585 kg of product. A preservative treatment with a combination of ascorbic and citric acid will limit the public health risk even if the potato product is accidentally **stored** for a short time at a **temperature** higher than 4°.

L45 ANSWER 9 OF 20 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 81168134 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6783645
TITLE: Separation and characterization of heavy and light chains from Clostridium **botulinum** type C **toxin** and their reconstitution.
AUTHOR: Syuto B; Kubo S
SOURCE: Journal of biological chemistry, (1981 Apr 25) 256 (8) 3712-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198106
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19810623

AB Clostridium **botulinum** type C **toxin** consists of a heavy and a light chain with molecular weights of 98,000 and 53,000, respectively, which are linked by one disulfide bond. The two components were separated from each other by quaternary aminoethyl

Sephadex A-50 column chromatography by stepwise elution with **NaCl** in 27.5 mM borax-45 mM sodium dihydrogen **phosphate buffer, pH** 8.0, containing 5% 2-mercaptoethanol at 0 degrees C. The purified components had different amino acid compositions and antigenicities, and the toxicity of the toxin was neutralized completely by either anti-heavy chain Fab or anti-light chain Fab. the two components could be reconstituted to form an active molecule with recovered toxicity which varied according to the method used. Maximum recovery was obtained in a system in which the intersubunit S--S bond was first formed in the presence of high concentration of neutral salts, after which the concentration of salt was gradually decreased. The reconstituted preparation was highly toxic and had the same properties as the parental toxin on chromatography, sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and immunodiffusion. By the use of three perturbants, the fractions of exposed tryptophans and tyrosines of the preparation were found to be almost the same as that of the parental toxin.

L45 ANSWER 10 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:87608 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA09407042392A
TITLE: Isolation and properties of highly purified type **F** Clostridium **botulinum toxin**
AUTHOR(S): Uvarova, R. N.; Reshetnikova, L. N.; Ispolatovskaya, M. V.; Bulatova, T. I.
CORPORATE SOURCE: Inst. Epidemiol. Mikrobiol., Moscow, USSR.
SOURCE: Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii, (1980) No. 11, pp. 42-6.
CODEN: ZMEIAV. ISSN: 0372-9311.
COUNTRY: USSR
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1981:42392
LANGUAGE: Russian
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021203

AB The steps involved in the isolation of C. **botulinum toxin** were initial precipitation with (NH4)2SO4 or Na hexametaphosphate after cultivation of the culture for 4 days at 28°, ultrafiltration through amicon membrane, gel filtration on 2 sephadex G-100 columns and elution with **pH** 5.6 Na **phosphate-phosphate buffer,** chromatog. on DEAE-cellulose, dialysis in a **pH** 4.2 **acetate buffer** containing 0.1 M **NaCl,** chromatog. on SP-sephadex (C-50), repeating of dialysis, ultrafiltration and then gel filtration on sephadex G-200, and finally dialysis and chromatog. on DEAE-cellulose. The activity of the purified toxin ranged 1.5-4 + 107 (min. LD)/mg protein and had a mol. weight of 50,000 daltons.

L45 ANSWER 11 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:104152 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA09115118322P
TITLE: Structure and toxicity of Clostridium **botulinum** type C **Toxin**

AUTHOR(S): Syuto, Bunei; Kubo, Shuichiro
CORPORATE SOURCE: Fac. Vet. Med., Hokkaido Univ., Sapporo, 060, Japan.
SOURCE: Japanese Journal of Medical Science & Biology, (1979) Vol. 32, No. 2, pp. 132-3.
CODEN: JJMCAQ. ISSN: 0021-5112.
COUNTRY: JAPAN
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1979:518322
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021210

AB C. **botulinum Toxin** C could be separated into 2 peptide chains by chromatog. of QAE-Sephadex A-50 with a linear gradient of **NaCl** in 6% 2-mercaptoethanol-borate **phosphate buffer** at **pH** 8.1 and 0°. The components had different antigenicities and antitoxin to either chain neutralized the mother toxin toxicity. Combining the 2 chains gave an active form having 74% of the toxicity of the mother toxin; thus both chains are essential for toxicity. The reconstitution method affected the toxicity of the material prepared from the chains. Tryptophan and tyrosine residues were critical to maintain the toxin toxicity.

L45 ANSWER 12 OF 20 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 76202136 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5836
TITLE: [Extraction and concentration of Clostridium **botulinum toxins** from specimens (author's transl)].
Extraktion und Anreicherung von Clostridium botulinum-Toxinen aus dem Untersuchungsmaterial.
AUTHOR: Sonnenschein B; Bisping W
SOURCE: Zentralblatt fur Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. Erste Abteilung Originale. Reihe A: Medizinische Mikrobiologie und Parasitologie, (1976 Mar) 234 (2) 247-59.
Journal code: 0331570. ISSN: 0300-9688.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197608
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19760802

AB In order to detect minimal amounts of Clostridium **botulinum toxins** in animal tissue or food specimens it is necessary to use an extraction method which results in concentration of the **botulinal toxins**. In the present examinations, artificially contaminated canned beans were used to develop a suitable procedure for extraction and concentration of **botulinal toxins A-E**. The procedure consisted of 4 steps: 1. Canned beans were diluted 1:2 with 0.1 m **phosphate buffer pH** 6.0. 2. The diluted material was homogenised with an "Ultra-Turrax" homogeniser for 20 sec. 3. The monogenised material was centrifuged at 4000 rpm for 30 min. 4. 15 ml of supernatant was concentrated using a "Millipore ultrafiltration chamber" (with a membrane capable of excluding all material with a molecular weight above 25,000). A pressure of 1.5 atmospheres was

applied until the terminal volume was 0.5 ml. Following extraction and concentration, the samples were assayed for **botulinal toxin** in mice. Using this assay the concentration of the five toxins were shown to be as follows: Type A toxin: 19.0-fold toxin concentration Type B toxin: **14**.8-fold toxin concentration Type C toxin: 20.6-fold toxin concentration Type D toxin: 28.2-fold toxin concentration Type E toxin: 112.2-fold toxin concentration

L45 ANSWER 13 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 6

ACCESSION NUMBER: 1977:137266 BIOSIS
DOCUMENT NUMBER: PREV197763032130; BA63:32130
TITLE: THE MICROBIOLOGICAL ROLE OF NITRITE AND NITRATE.
AUTHOR(S): ROBERTS T A
SOURCE: Journal of the Science of Food and Agriculture, (1975) Vol. 26, No. 11, pp. 1755-1760. CODEN: JSFAAE. ISSN: 0022-5142.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

AB In unheated products nitrite, **NaCl** and the pH value contribute to the selection of the bacteria which grow during **storage**. Nitrate is generally believed to serve only as a reservoir for nitrite, but the commercial use of nitrate-free cover brines in the Wiltshire bacon industry shows that such a reservoir is not always essential. Nitrate sometimes reduced the growth rate of bacteria in experimental Wiltshire collar bacon, but had no benefit in back bacon. The clostridia occurring naturally in the bacon grew to higher numbers in collar cured without nitrate than that cured with nitrate. Clostridium **botulinum** (types **A** and **B**) was detected in these bacons, but did not grow in the bacon. In heated products the growth of surviving bacteria is controlled by the interaction of several factors including pH, **NaCl storage temperature** and NaNO2 or a substance derived from it upon heating. Further experiments are warranted to investigate the effects of dextrose, nitrate, ascorbate and polyphosphate.

L45 ANSWER 14 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:82497 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA08623169232P
TITLE: Effect of additional concentration and purification on the antigenic activity and chemical composition of toxoids for use in aerosol vaccines
AUTHOR(S): Shipulina, N. I.; Vasil'eva, I. P.; Didenko, L. A.; Shapareva, S. I.; Karpov, S. P.
CORPORATE SOURCE: Tomsk. Nauchno-Issled. Inst. Vaktsin Syvorotok, Tomsk, USSR.
SOURCE: Trudy - Tomskii Nauchno-Issledovatel'skii Institut Vaktsin i Syvorotok, Tomskii Meditsinskii Institut [i] Tomskoe Otdelenie Vserossiiskogo Nauchno-Meditsinskogo Obshchestva Mikrobiologov, Epidemiologov i Parazitologov, (1975) Vol. 25, pp. 159-63. CODEN: TTVMA9. ISSN: 0130-4917.
COUNTRY: USSR
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1977:169232

LANGUAGE: Russian
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021218

AB The toxoids of Clostridium **botulinum** type **A**, **B**, and E were purified by precipitation at **pH** 3.3-3.5 and dialysis against **phosphate buffer pH** 6.81. C. tetani toxoids were precipitated with 15% **NaCl** and dialyzed against water. The content of Ca, Na, K, SO42-, B, P, and Cl decreased below those of starting crude toxoids. The antigenic activity and stability during storage also decreased after the purification

L45 ANSWER 15 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1974:67187 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA080019105759J
TITLE: Germination of spores of Clostridium species capable of causing food poisoning. II. Effects of some chemicals on the germination of spores of C. **botulinum** type **A**
AUTHOR(S): Ando, Yoshiaki
CORPORATE SOURCE: Hokkaido Inst. Public Health, Sapporo, Japan.
SOURCE: Shokuhin Eiseigaku Zasshi, (1973) Vol. 14, No. 5, pp. 462-6.
CODEN: SKEZAP. ISSN: 0015-6426.
COUNTRY: JAPAN
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1974:105759
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021218

AB Spores of C. **botulinum** type **A** 190 were heated at 70° for 10 min in 250mM **phosphate buffer pH** 6.7, cooled, and then incubated at 37° in germination medium containing 5mM L-alanine, 10mM Na L-lactate, 60mM NaHCO3, and 100mM **phosphate buffer pH** 6.7. Addition of 150mM D-alanine prevented germination. Addition of ≥5% **NaCl** or ≥1% Na sorbate to the medium retarded germination. EDTA, dipicolinic acid, and 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide showed no effect.

L45 ANSWER 16 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:50680 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA070019085842U
TITLE: Purification and molecular dissociation of the precursor of Clostridium **botulinum** type **E toxin**
AUTHOR(S): Kitamura, Masaru; Sakaguchi, Simiko; Sakaguchi, Genji
CORPORATE SOURCE: Nat. Inst. Health, Tokyo, Japan.
SOURCE: Anaerobic Bact., Proc. Int. Workshop, 5th, (1968) pp. 213-22.
CODEN: 20QCAI.
COUNTRY: JAPAN
DOCUMENT TYPE: Conference
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1969:85842
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116

Last Updated on STN: 20021231

AB The **toxin** of C. **botulinum** type **E** is formed as a nontoxic ribonucleoprotein (I) which can be extracted from the cells with 0.2M **phosphate buffer, pH** 6.0. The protein moiety is purified by precipitation of I by half-saturated (NH4)2SO4, chromatog. on CM-Sephadex C-50 (II) at **pH** 6.0 (0.02M **acetate buffer**), digestion with RNase, rechromatog. on II at **pH** 6.0 with a linear concentration gradient of **NaCl** in 0.02M **acetate buffer**, precipitation by half-saturated (NH4)2SO4, chromatog. on Sephadex G-200, and rechromatog. on II. The toxicity of the product for mice was 2-8 LD50/mg. N, but activation by trypsin raised this to 5-10 LD50/mg. N. The material appeared homogeneous on disk electrophoresis (**pH** 4) and on ultracentrifugation (**pH** 4.5 or 6.0, s20, W 11.3-12.3 S), but gave 2 distinct precipitin lines on immunodiffusion and 2 distinct zones on electrophoresis (cellulose **acetate**) at **pH** 7. Ultracentrifugation at **pH** 8 (0.05M Veronal **buffer**) gave a single major band, s20, W 7.3 S. Starch-gel electrophoresis at **pH** 8 (0.05M Veronal **buffer**) gave partial separation into anodic and cathodic peaks; only the latter gave active toxin after treatment with trypsin.

L45 ANSWER 17 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1968:24747 TOXCENTER
COPYRIGHT:	Copyright 2005 ACS
DOCUMENT NUMBER:	CA06805020941Q
TITLE:	Demonstration of bacterial toxins in foodstuffs by means of immunofluorescence
AUTHOR(S):	Riemann, Hans
CORPORATE SOURCE:	Sch. of Vet. Med., Univ. of California, Davis, CA, USA.
SOURCE:	Nordisk Veterinaermedicin, (1967) Vol. 19, No. 4, pp. 188-94. CODEN: NOVTAV. ISSN: 0029-1579.
COUNTRY:	UNITED STATES
DOCUMENT TYPE:	Journal
FILE SEGMENT:	CAPLUS
OTHER SOURCE:	CAPLUS 1968:20941
LANGUAGE:	Danish
ENTRY DATE:	Entered STN: 20011116 Last Updated on STN: 20021231

AB Staphylococcal enterotoxin B antitoxin, obtained from rabbits, was conjugated with fluorescein isothiocyanate and purified on DEAE-cellulose and Sephadex columns. The conjugate was adsorbed to nontoxin-producing staphylococcal strains and purified as Sephadex. To avoid false neg. results due to extracellular localization of toxin, the conjugate and culture, after incubation at 30° for 30 min. and at 20° for 4 hrs., were filtered through a 0.22-μ pore filter plus Whatman Number 1 filter paper. Direct preparates were prepared by growing cultures on dialysis membranes mounted on blood-agar. The preparate was freeze-dried and colored by incubation with conjugate at 37°. With these methods 1 γ toxin/ml. sample was detected. In a quant. modification, antiserum and agar were mixed (50:50) and poured into small glass tubes. Test solution was pipetted on the gel and after 1-7 days incubation, the amount of toxin was estimated, being related to the distance between the surface and the line of precipitation With this method 4 γ/ml. were detectable after 8 days and 8 γ/ml. after 1 day. The toxin was identified by gel-diffusion technique. These methods were used for determination of

toxin in various foods. It was found that 1-10 γ toxin was formed per g. ham on anaerobic **storage** for 8-13 days at room **temperature** The amount of toxin formed varied according to **pH** and salt concentration At **pH** 6.9 and **NaCl** concentration 10-12 g./100 ml. and **pH** 5.1 and **NaCl** concentration 4 g./100 ml. both totally inhibited production of toxin. Com. Clostridium **botulinum E** antiserum was purified by precipitation with (NH4)2SO4 and chromate on Sephadex and in two steps adsorbed to nontoxin-producing and **toxin**-producing C. **botulinum E**. Com. rabbit antihorse serum γ-globulin, conjugated with fluorescein isothiocyanate was dialyzed against a **phosphate buffer** and chromatographed on a DEAE-cellulose column. Preparates were incubated with antitoxin for 0.5-1 hr. at 37° and again under the same conditions with rabbit antihorse serum. Neither nontoxic strain E nor strain A or B or pseudobotulinum E from toxic cultures of strain E showed fluorescence with reagent. Toxic cultures of strain E showed no fluorescence when tested against antitoxin A or B. Incubations of ham showed, when tested on mice, that toxin was produced when the salt concentration decreased under 2.5 g./100 ml. H2O; these expts., however, were neg. to the fluorescence being described.

L45 ANSWER 18 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:14272 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA05608045110H
TITLE: Decontamination of drinking water with mobile equipment
AUTHOR(S): Mehls, Karl F. H.
SOURCE: GWF, das Gas- und Wasserfach, (1961) Vol. 102, pp. 1365-9.
CODEN: GAWFAN. ISSN: 0367-3839.
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1962:45110
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20031104

AB This is an abridgment of an article to be published as a Dechema monograph. A discussion is presented of the field use of mobile equipment to remove radioactivity, bacteria, viruses, botulins, and war gases from drinking water. In general, better results are secured by adding filter material, reagents, etc., to the water than by using fixed filter beds. Kieselguhr can be treated with Ag to have a bactericidal effect. Cl kills bacteria and viruses and destroys biol. warfare materials such as the **botulinus toxins** in **a** few min. This is most conveniently supplied as NaClO from the electrolysis of **NaCl** solns., although Ca(ClO)2 can also be used. Where war gases such as **phosphate** esters, are present, these can be removed by hydrolysis at a high pH in the presence of hypochlorite. Adsorption followed by precipitation and the use of flocculants is also suggested. Radioactivity can readily be removed by mixed-bed deionization filters, but the mixed-bed resin deteriorates with time, especially when **stored** at elevated **temps**. Handling of the contaminated resin and regeneration is also a problem. M. uses a cation exchanger operating on a Na cycle. Patent coverage on decontamination processes is cited.

L45 ANSWER 19 OF 20 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1947:348 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA04105006248E
TITLE: Molecular weight and homogeneity of crystalline **botulinus A toxin**
AUTHOR(S): Putnam, Frank W.; Lamanna, Carl; Sharp, D. G.
CORPORATE SOURCE: Camp Detrick, Frederick, MD.
SOURCE: Journal of Biological Chemistry, (1946) Vol. 165, pp. 735-6.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1947:6248
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20030624

AB cf. C.A. 40, 4767.2, 6121.2. The electrophoretic, sedimentation, and diffusion characteristics of crystalline Clostridium **botulinum** type **A toxin** have been studied in 0.1 N Na **acetate buffer, pH** 4.38. The toxin is electrophoretically homogeneous and has a mobility of 2.75 + 10-5 sq. cm. volt-1 sec.-1. The ultracentrifugal sedimentation diagrams show a single symmetrical boundary and yield a value of S20 = 17.3 Svedberg units. The diffusion constant of a 0.63% solution at 25° by the refractometric scale method is 2.**14** + 10-7 sq. cm. sec.-1. Satisfactory agreement at successive time intervals among the values calculated by different methods and a good fit of the normalized diffusion curves with the ideal distribution curve have been realized. The boundary spread in the ultracentrifuge is greater than that attributable to diffusion alone. If a partial sp. volume of 0.75 is assumed, the mol. weight calculated from S20 and D20 is 900,000 (cf. C.A. 40, 6560.1); this suggests the presence of 2.1 + 107 mols. per mouse LD50. A tentative frictional value of 1.76 is assigned. If the mols. are assumed to be prolate elipsoids, this figure corresponds to an axial ratio, b/a = **14**.6, neglecting hydration.

L45 ANSWER 20 OF 20 FEDRIP COPYRIGHT 2005 NTIS on STN
ACCESSION NUMBER: 2005:135428 FEDRIP
NUMBER OF REPORT: AGRIC 0187659
RESEARCH TITLE: ENZYMOLOGY OF MICROBIAL DEGRADATION OF ORGANIC COMPOUNDS
STAFF: Principal Investigator: (x ray crystallography) Chase, T.
PERFORMING ORGN: RUTGERS UNIVERSITY, BIOCHEMISTRY & MICROBIOLOGY, NEW BRUNSWICK, NEW JERSEY, 08903
FUNDING: HATCH |c H
FILE SEGMENT: Department of Agriculture

SUM To determine characteristics (substrate specificity, kinetic mechanism, native subunit structure) of microbial enzymes involved in degradation of polluting organic compounds. Enzymes to be studied include aromatic alcohol:NAD oxyoreductase, nitrobenzoate reductase, hydroxylaminobenzoate lyase, and gentisate and 1-hydroxy-2-naphthoate oxygenases. To identify the activity of an unidentified gene product linked to aromatic alcohol dehydrogenase, and thus to determine what compounds these enzymes make the organism ableto degrade. The enzymes, which have been cloned, will be expressed in Escherichia coli, and substrate specificity survayed in crude extracts. Enzymes then will be purified for study of the kinetic characteristics and mechanism on

selected substrates, native molecular weight determination by gel filtration, and possible X-ray crystallographic determination of structure. Kinetic studies will include variation of concentration of both substrates and use of product and dead-end inhibitors. The function of an unidentified gene product will be investigated by insertion of an intervening sequence into the chromosomal gene and observation of loss of ability to grow on some substrates, to suggest enzymatic function of the gene product.PR pseudoalcaligenes JS45, expressed in E. coli, have been purified to near homogeneity. Kinetic study of the YH105 reductase, varying concentrations of both 4-nitrobenzoate and NADPH, showed a sequential mechanism (intersecting plots of 1/v vs. 1/NADPH]) and substrate inhibition at [4-nitrobenzoate] above 0.25 mM. This contrasts with known nitroaromatic reductases such as that of Escherichia coli, which have ping-pong mechanisms, NADPH reducing the bound FMN which subsequently reduces the substrate. The limiting Michaelis constant for 4-nitrobenzoate is 0.0326+/-0.004 mM, and for NADPH 0.0154+/-.00375 mM. The substrate inhibition is competitive vs. NADPH, i.e. slopes of plots of 1/v vs. 1/[NADPH] increase again at higher 4-nitrobenzoate concentrations. The nitroaromatic reductase of Ralstonia eutropha JMP134 similarly shows a sequential mechanism, limiting Michaelis constant for 3-nitrophenol = 2.43+/-0.**14** micromolar, for NADPH 9.61+/-1.3 micromolar. Comparison of 4-nitrophenol and 4-nitrosophenol (the intermediate product/substrate of the 4-electron reduction) at **pH** 5.8 (where both are predominantly neutral) also showed a sequential mechanism, 4-nitrosphenol having a much lower Michaelis constant, and both showing substrate inhibition above 0.25 mM. Thus substrate inhibition is not a feature only of the four-electron, two-NADPH reduction. The purified YH105 enzyme appears to be active without FMN, unlike other nitroaromatic reductases (including those of JS45 and JMP134). Kinetic study of the JS45 enzyme has not proceeded as far (the Michaelis constant for NADPH is high, above 0.2 mM, and for nitrobenzene very low), but it has been found that the enzyme is five times as active in **phosphate buffer** as in MOPS (3-morpholinopropanesulfonic acid). The other enzymes show slightly higher activity in **phosphate**. The hydroxylaminobenzoate lyase of YH105, like that of Comamonas acidovorans NBA-10 (Groenewegen, P.E.J., and de **Bont**, J.A.M., Arch. Microbiol. 158:381-6 [1992]) is stabilized by NADH. In an attempt to find the function of cinnamyl alcohol dehydrogenase of Burkholderia cepacia DBO-1 (a similar gene is found in E. coli and other microrganisms), we have been trying to knock out the gene by insertion of a kanamycin resistance cassette. At least one mutant has been obtained. It grows on aromatic substrates (phthalate, coumarate, benzyl alcohol, phenylalanine) only when supplemented with yeast extract, unlike the wild type organism, suggesting a possible role in coenzyme biosynthesis.PB

FILE 'MEDLINE' ENTERED AT 12:12:12 ON 27 OCT 2005

FILE LAST UPDATED: 26 OCT 2005 (20051026/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

Searcher : Shears 571-272-2528

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L46        4451 SEA FILE=MEDLINE ABB=ON  PLU=ON  "BOTULINUM TOXINS"/CT
L47       39392 SEA FILE=MEDLINE ABB=ON  PLU=ON  PHOSPHATES/CT
L48        1435 SEA FILE=MEDLINE ABB=ON  PLU=ON  "SUCCINIC ACID"/CT
L49       15019 SEA FILE=MEDLINE ABB=ON  PLU=ON  ACETATES/CT
L50       11647 SEA FILE=MEDLINE ABB=ON  PLU=ON  CITRATES/CN
L51           7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L46 AND (L47 OR L48 OR
                 L49 OR L50)
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L51 ANSWER 1 OF 7 MEDLINE on STN

ACCESSION NUMBER: 89264465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2471189
TITLE: Granulocyte-macrophage colony-stimulating factor and human neutrophils: role of guanine nucleotide regulatory proteins.
AUTHOR: Gomez-Cambronero J; Yamazaki M; Metwally F; Molski T F; Bonak V A; Huang C K; Becker E L; Sha'afi R I
CORPORATE SOURCE: Department of Physiology, University of Connecticut Health Center, Farmington 06032.
CONTRACT NUMBER: AI-09648 (NIAID)
AI-24935 (NIAID)
GM-37694 (NIGMS)
+
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1989 May) 86 (10) 3569-73. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 20021218
Entered Medline: 19890628

ED Entered STN: 19900309
Last Updated on STN: 20021218
Entered Medline: 19890628

AB The addition of granulocyte-macrophage colony-stimulating factor (GM-CSF) to human neutrophils causes a rapid increase in the basal and fMet-Leu-Phe-stimulated Na+ influx and an increase in intracellular pH. The increase can be seen as early as 5 min after the addition of GM-CSF. Changes produced by GM-CSF are totally inhibited by amiloride and are significantly reduced in pertussis toxin-treated cells. The stimulation of the Na+/H+ exchange mechanism by GM-CSF inhibits further stimulation of this system with either fMet-Leu-Phe or phorbol 12-myristate 13-acetate. In addition, membrane preparations isolated from GM-CSF-treated neutrophils have higher basal and stimulated GTPase activities. The basal and the fMet-Leu-Phe- or platelet-activating factor-stimulated GTPase activities are reduced in pertussis toxin-treated cells. Cells pretreated with GM-CSF accumulate more radioactive phosphate than control cells, and this

increase is diminished by pertussis toxin treatment. In addition, GM-CSF causes a rapid increase in the tyrosine phosphorylation levels of five proteins with molecular masses of 118 kDa, 92 kDa, 78 kDa, 54 kDa, and 40 kDa. These results clearly show that GM-CSF, on its own, can initiate several changes and that these changes are mediated in part by the pertussis toxin-sensitive guanine nucleotide regulatory protein.

L51 ANSWER 2 OF 7 MEDLINE on STN
ACCESSION NUMBER: 87190484 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3569302
TITLE: Botulinum C2 toxin ADP-ribosylates actin and disorganizes the microfilament network in intact cells.
AUTHOR: Reuner K H; Presek P; Boschek C B; Aktories K
SOURCE: European journal of cell biology, (1987 Feb) 43 (1) 134-40.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198705
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870528
ED Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870528
AB Botulinum C2 toxin ADP-ribosylates actin in [32P]orthophosphate-labelled intact chick embryo cells (CEC). The toxin-induced rounding up of CEC is correlated with ADP-ribosylation of actin in intact cells in a time and concentration-dependent manner. Both, rounding up of cells and actin ADP-ribosylation, depend on the presence of both components of botulinum C2 toxin (components I and II) and are independent of the ability of CEC to divide. Treatment of CEC with botulinum C2 toxin induced a time-dependent disorganization of the typical architecture of the microfilament network as shown by fluorescein-phalloidin staining. Botulinum C2 toxin decreased the amount of Triton X-100 insoluble actin, while the fraction of Triton soluble actin was increased. Actin, which was 32P-labelled by botulinum C2 toxin in intact CEC, was recovered in the Triton soluble but not in the Triton insoluble actin fraction. It is suggested that in intact CEC botulinum C2 toxin causes ADP-ribosylation of G-actin but not of F-actin thereby leading to an accumulation in the pool of monomeric actin.

L51 ANSWER 3 OF 7 MEDLINE on STN
ACCESSION NUMBER: 85278125 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2992374
TITLE: Inhibition of Clostridium botulinum 52A toxicity and protease activity by sodium acid pyrophosphate in media systems.
AUTHOR: Wagner M K; Busta F F
SOURCE: Applied and environmental microbiology, (1985 Jul) 50 (1) 16-20.
Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

Searcher : Shears 571-272-2528

FILE SEGMENT: Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850916

ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19850916

AB The effects of two pH levels (5.55 or 5.85) in combination with 0.4% sodium acid pyrophosphate (SAPP), NaH2PO4 X H2O, Na2HPO4 X 7H2O, or NaCl on the growth and toxicity of Clostridium botulinum 52A were studied. Absorbancy measurements at 630 nm, microscopic observations, and the mouse bioassay procedure were used to observe the effects. At pH 5.55 and 5.85 most control cultures exhibited toxicity when cell lysis began. Vegetative cell development was normal (4 micron long; 1 micron wide). SAPP-containing (0.4%) treatment cultures displayed similar growth and lysis but no or delayed (48 h) toxicity. Cells grown in the SAPP treatment culture were longer and wider (6 micron long; 1.5 micron wide) than in most other treatment cultures. Trypsinization of nontoxic supernatants from 0.4% SAPP resulted in toxicity. Addition of 0.4% SAPP to toxic C. botulinum supernatant delayed but did not prevent death of mice. The addition of various levels of SAPP to toxic supernatants resulted in a decrease in zone size with an increase in the level of SAPP (9 mm with 0.4% SAPP to 7 mm with 1.0% SAPP), using a dual substrate protease assay. A decrease in the zone size also occurred with the supernatant from cultures grown in the presence of SAPP and with Bacillus polymyxa protease dilutions containing 0.4% SAPP. Results suggest that the actual production or function of the protease responsible for toxin activation may have been inhibited by the presence of SAPP.

L51 ANSWER 4 OF 7 MEDLINE on STN
ACCESSION NUMBER: 73221663 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4719441
TITLE: Disulfide-toxicity relationship of botulinal toxin types A, E, and F.
AUTHOR: Sugiyama H; Das Gupta R; Yang K H
SOURCE: Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N. Y.), (1973 Jul) 143 (3) 589-91.
Journal code: 7505892. ISSN: 0037-9727.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197309
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19730924

ED Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19730924

L51 ANSWER 5 OF 7 MEDLINE on STN
ACCESSION NUMBER: 73026881 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4342990
TITLE: Ultrastructural studies of the effects of various agents on the motor neurons of the spinal cord.
AUTHOR: Yates R D; Yates J C

SOURCE: American journal of anatomy, (1972 Nov) 135 (3) 345-57.
Journal code: 0376312. ISSN: 0002-9106.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197301
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19730103
ED Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19730103

L51 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 72092593 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4944802
TITLE: Heat resistance of spores of marine and terrestrial strains of Clostridium botulinum type C.
AUTHOR: Segner W P; Schmidt C F
SOURCE: Applied microbiology, (1971 Dec) 22 (6) 1030-3.
Journal code: 7605802. ISSN: 0003-6919.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197204
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19720404
ED Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19720404

L51 ANSWER 7 OF 7 MEDLINE on STN
ACCESSION NUMBER: 70107475 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4312998
TITLE: A study of the effect of ionizing radiation on resistance, germination, and toxin synthesis of Clostridium botulinum spores, types A, B, and E. COO-1095-3.
AUTHOR: Graikoski J T; Kempe L L
SOURCE: COO [reports]. U. S. Atomic Energy Commission, (1966 Jan 14) 1-100.
Journal code: 21830370R.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197003
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19970203
Entered Medline: 19700322
ED Entered STN: 19900101
Last Updated on STN: 19970203
Entered Medline: 19700322

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 12:14:47 ON 27 OCT 2005)

- Author(s)

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L52          512 S "MOYER E"?/AU
L53           37 S "HIRTZER P"?/AU
L54            3 S L52 AND L53
L55            3 S (L52 OR L53) AND L28
L56            3 S L54 OR L55
L57            1 DUP REM L56 (2 DUPLICATES REMOVED)
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L57 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2000:190943 CAPLUS
DOCUMENT NUMBER: 132:227422
TITLE: Stable liquid formulations of **Botulinum toxin**
INVENTOR(S): **Moyer, Elizabeth; Hirtzer, Pamela**
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015245	A2	20000323	WO 1999-US20912	19990909
WO 2000015245	A3	20000608		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
TW 574036	B	20040201	TW 1999-88114941	19990831
CA 2342243	AA	20000323	CA 1999-2342243	19990909
AU 9958214	A1	20000403	AU 1999-58214	19990909
AU 755556	B2	20021212		
BR 9913585	A	20010605	BR 1999-13585	19990909
EP 1112082	A2	20010704	EP 1999-945649	19990909
EP 1112082	B1	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100728	T2	20010821	TR 2001-200100728	19990909
SI 20566	C	20011231	SI 1999-20081	19990909
EE 200100140	A	20020617	EE 2001-140	19990909
JP 2002524527	T2	20020806	JP 2000-569829	19990909
AT 221386	E	20020815	AT 1999-945649	19990909
ES 2181473	T3	20030216	ES 1999-945649	19990909
NZ 509349	A	20030829	NZ 1999-509349	19990909
ZA 2001001709	A	20021128	ZA 2001-1709	20010228
NO 2001001207	A	20010509	NO 2001-1207	20010309
LV 12684	B	20011020	LV 2001-56	20010410
BG 105435	A	20011231	BG 2001-105435	20010410
LT 4959	B	20021025	LT 2001-41	20010410
PRIORITY APPLN. INFO.:			US 1998-99870P P	19980911

WO 1999-US20912 W 19990909

AB The invention includes liquid formulations of **botulinum toxin** that are stable to storage in liquid form at standard refrigerator temps. for at least 1-2 yr and to storage at higher temps. for at least 6 mo. The invention also includes methods of treatment using such formulations and uses of such formulations in the manufacture of medicaments for various therapeutic and cosmetic treatments. A formulation was prepared containing **Botulinum toxin** Type **B** 500±100 LD50U/mL, di-Na **succinate** 10 mM, NaCl 100 mM, human albumin 0.5 mg/mL, and HCl for pH adjustment.

FILE 'HCAPLUS' ENTERED AT 14:53:15 ON 27 OCT 2005

-key terms w/ corrected L# for NaCl RN

```
L58            17 S L28 AND L14
L59             2 S L58 AND (L24 OR HSA OR ALBUMIN OR GELATIN)
L60             4 S L58 AND BUFFER?
L61             1 S L60 AND (TEMP OR TEMPERATURE)
L62             0 S (L59 OR L61) NOT (L30 OR L36)
```

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 14:53:52 ON 27 OCT 2005

```
L63             4 S L59
L64             1 S L61
L65             0 S (L63 OR L64) NOT (L32 OR L44)
```

FILE 'HOME' ENTERED AT 14:59:15 ON 27 OCT 2005

Searcher : Shears 571-272-2528

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=> d his ful

     (FILE 'HOME' ENTERED AT 11:40:58 ON 27 OCT 2005)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 11:41:09 ON 27 OCT 2005
               E BOTOX/CN 5
L1             1 SEA ABB=ON  PLU=ON  BOTOX/CN
               D CN
               E BOTULIN TOXIN/CN 5
L2             6 SEA ABB=ON  PLU=ON  BOTULIN TOXIN? /CN
L3             8 SEA ABB=ON  PLU=ON  BOTULIN NEUROTOXIN? /CN
L4             8 SEA ABB=ON  PLU=ON  BOTULINUM TOXIN? /CN
L5            14 SEA ABB=ON  PLU=ON  BOTULINUM NEUROTOXIN? /CN
L6           134 SEA ABB=ON  PLU=ON  (BOTULIN A ? OR BOTULIN B ? OR BOTULIN
                 C1 ? OR BOTULIN C2 ? OR BOTULIN D ? OR BOTULIN E ? OR
                 BOTULIN F ?)/CN
L7             2 SEA ABB=ON  PLU=ON  (BOTULINUM A ? OR BOTULINUM B ? OR
                 BOTULINUM C1 ? OR BOTULINUM C2 ? OR BOTULINUM D ? OR
                 BOTULINUM E ? OR BOTULINUM F ?)/CN
L8           156 SEA ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7

               E PHOSPHATE/CN
L9             9 SEA ABB=ON  PLU=ON  (PHOSPHATE/CN OR "PHOSPHATE (32PO4)"/CN
                  OR "PHOSPHATE (H2PO4-)"/CN OR "PHOSPHATE (H2PO41-)"/CN OR
                 "PHOSPHATE (HPO42-)"/CN OR "PHOSPHATE (P2O74-)"/CN OR
                 "PHOSPHATE (P4O123-)"/CN) OR "PHOSPHATE (P6O186-)"/CN OR
                 ("PHOSPHATE (PO3-)"/CN OR "PHOSPHATE (PO31-)"/CN OR
                 "PHOSPHATE (PO32-)"/CN) OR "PHOSPHATE (PO43-)"/CN OR
                 "PHOSPHATE (PO4H2-)"/CN
               E CITRATE/CN 5
L10            1 SEA ABB=ON  PLU=ON  CITRATE/CN
               E ACETATE/CN 5
L11            1 SEA ABB=ON  PLU=ON  ACETATE/CN
               E SUCCINATE/CN 5
L12            1 SEA ABB=ON  PLU=ON  SUCCINATE/CN
               D CN
L13           12 SEA ABB=ON  PLU=ON  L9 OR L10 OR L11 OR L12
L14          445 SEA ABB=ON  PLU=ON  SODIUM CHLORIDE ?/CN
               E BONT/CN 5

     FILE 'HCAPLUS' ENTERED AT 11:45:22 ON 27 OCT 2005

     FILE 'REGISTRY' ENTERED AT 11:47:35 ON 27 OCT 2005
L15            6 SEA ABB=ON  PLU=ON  (BOTULIN G ? OR BOTULINUM G ?)/CN
L16          161 SEA ABB=ON  PLU=ON  L8 OR L15

     FILE 'HCAPLUS' ENTERED AT 11:47:44 ON 27 OCT 2005
L*** DEL    3892 S L16 OR (BO BOTULIN?)(5A)(NT OR TOXIN OR NEUROTOXIN OR TOX
L17         4721 SEA ABB=ON  PLU=ON  L16 OR (BO OR BOTULIN?)(5A)(NT OR
                 TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR BOTX#
                 OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(3A)(A OR B OR
                 C1 OR C2 OR D OR E OR F OR G)
L18      1354347 SEA ABB=ON  PLU=ON  L13 OR PHOSPHATE OR CITRATE OR ACETATE
                 OR SUCCINATE OR SUCCINIC OR BUTANEDIOIC OR ACETIC
L19          246 SEA ABB=ON  PLU=ON  L17 AND L18
L20           63 SEA ABB=ON  PLU=ON  L19 AND (14 OR NACL OR (NA OR SODIUM)(W
                 )(CL OR CHLORIDE) OR SALINE)
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     FILE 'REGISTRY' ENTERED AT 11:49:57 ON 27 OCT 2005
                E HUMAN SERUM ALBUMIN/CN 5
L21           3 SEA ABB=ON  PLU=ON  HUMAN SERUM ALBUMIN ?/CN
                E SERUM ALBUMIN/CN 5
L22          62 SEA ABB=ON  PLU=ON  SERUM ALBUMIN ?/CN
                E GELATINS/CN 5
L23           1 SEA ABB=ON  PLU=ON  GELATINS/CN
L24          66 SEA ABB=ON  PLU=ON  L21 OR L22 OR L23

     FILE 'HCAPLUS' ENTERED AT 11:50:43 ON 27 OCT 2005
L25           3 SEA ABB=ON  PLU=ON  L20 AND (L24 OR HSA OR SER## ALBUMIN
                OR GELATIN)
L26           8 SEA ABB=ON  PLU=ON  L20 AND (L24 OR HSA OR ALBUMIN OR
                GELATIN)

     FILE 'REGISTRY' ENTERED AT 11:52:32 ON 27 OCT 2005

     FILE 'HCAPLUS' ENTERED AT 11:52:32 ON 27 OCT 2005
                D QUE L26
                D L26 1-8 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN,
     TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 11:52:33 ON 27 OCT 2005

     FILE 'HCAPLUS' ENTERED AT 11:54:16 ON 27 OCT 2005
L27        6302 SEA ABB=ON  PLU=ON  L16 OR (BO OR BOTULIN?)(5A)(NT OR
                TOXIN OR NEUROTOXIN OR TOX#) OR BOTOX# OR BONT# OR BOTX#
                OR BTX# OR (BT OR BN OR BNT#)(S)BOTULIN? OR BOTULIN?(3A)(A
                OR B OR C1 OR C2 OR D OR E OR F OR G)
L28         290 SEA ABB=ON  PLU=ON  L27 AND L18
L29          66 SEA ABB=ON  PLU=ON  L28 AND (14 OR NACL OR (NA OR SODIUM)(W
                )(CL OR CHLORIDE) OR SALINE)
L*** DEL      3 S L29 AND (L24 OR HSA OR SER## ALBUMIN OR GELATIN)
L30           8 SEA ABB=ON  PLU=ON  L29 AND (L24 OR HSA OR ALBUMIN OR
                GELATIN)
                D QUE L30
L31           0 SEA ABB=ON  PLU=ON  L30 NOT L26

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN,
     TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 11:55:55 ON 27 OCT 2005
L32          16 SEA ABB=ON  PLU=ON  L30
L33          11 DUP REM L32 (5 DUPLICATES REMOVED)
                D 1-11 IBIB ABS

     FILE 'HCAPLUS' ENTERED AT 11:59:55 ON 27 OCT 2005
L34          22 SEA ABB=ON  PLU=ON  L29 AND BUFFER?
L35          16 SEA ABB=ON  PLU=ON  L29 AND (TEMP OR TEMPERATURE)
L36          28 SEA ABB=ON  PLU=ON  (L34 OR L35) NOT L30
                D KWIC
                D 1-28 IBIB ABS

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN,
     TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 12:02:38 ON 27 OCT 2005
L37          63 SEA ABB=ON  PLU=ON  L34
L38          46 SEA ABB=ON  PLU=ON  L35
L39          35 SEA ABB=ON  PLU=ON  L37 AND (PH OR (H OR HYDROGEN)(W) ION)

                D KWIC
L40           4 SEA ABB=ON  PLU=ON  L39 AND (TEMP OR TEMPERATURE)
```

```
                D KWIC
L41           0 SEA ABB=ON  PLU=ON  L38 AND CENTIGRADE
L42           0 SEA ABB=ON  PLU=ON  L38 AND CELSIUS
L43           9 SEA ABB=ON  PLU=ON  L38 AND (STORE# OR STORING OR STORAGE)

                D KWIC
L44          39 SEA ABB=ON  PLU=ON  (L39 OR L43) NOT L32
L45          20 DUP REM L44 (19 DUPLICATES REMOVED)
                D QUE L39
                D QUE L43
                D L45 1-20 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 12:12:12 ON 27 OCT 2005
                E BOTULINUM TOXINS/CT 5
L46        4451 SEA ABB=ON  PLU=ON  "BOTULINUM TOXINS"/CT
                E BOTULINUM NEUROTOXINS/CT 5
                E PHOSPHATES/CT 5
L47       39392 SEA ABB=ON  PLU=ON  PHOSPHATES/CT
                E SUCCINIC ACID/CT 5
L48        1435 SEA ABB=ON  PLU=ON  "SUCCINIC ACID"/CT
                E ACETATES/CT 5
L49       15019 SEA ABB=ON  PLU=ON  ACETATES/CT
                E CITRATE/CN 5
                E CITRATES/CN 5
L50       11647 SEA ABB=ON  PLU=ON  CITRATES/CN
L51           7 SEA ABB=ON  PLU=ON  L46 AND (L47 OR L48 OR L49 OR L50)
                D QUE
                D 1-7 .BEVERLYMED

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO,
     PHIC, PHIN, TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 12:14:47
     ON 27 OCT 2005
L52         512 SEA ABB=ON  PLU=ON  "MOYER E"?/AU
L53          37 SEA ABB=ON  PLU=ON  "HIRTZER P"?/AU
L54           3 SEA ABB=ON  PLU=ON  L52 AND L53
L55           3 SEA ABB=ON  PLU=ON  (L52 OR L53) AND L28
L56           3 SEA ABB=ON  PLU=ON  L54 OR L55
L57           1 DUP REM L56 (2 DUPLICATES REMOVED)
                D IBIB ABS

     FILE 'HOME' ENTERED AT 12:19:21 ON 27 OCT 2005
                D COST

     FILE 'HCAPLUS' ENTERED AT 14:43:46 ON 27 OCT 2005
L*** DEL     17 S L19 AND L14
L*** DEL      2 S L58 AND (L24 OR HSA OR ALBUMIN OR GELATIN)
L*** DEL      4 S L58 AND BUFFER?
L*** DEL      1 S L60 AND (TEMP OR TEMPERATURE)
L*** DEL     17 S L28 AND L14
L*** DEL      2 S L58 AND (L24 OR HSA OR ALBUMIN OR GELATIN)
L*** DEL      4 S L58 AND BUFFER?
L*** DEL      1 S L60 AND (TEMP OR TEMPERATURE)
L*** DEL      0 S (L59 OR L61) NOT (L30 OR L36)

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN,
     TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 14:49:14 ON 27 OCT 2005
L*** DEL      4 S L59
                D QUE L14
```

```
     FILE 'HCAPLUS' ENTERED AT 14:53:15 ON 27 OCT 2005
L58           17 SEA ABB=ON  PLU=ON  L28 AND L14
L59            2 SEA ABB=ON  PLU=ON  L58 AND (L24 OR HSA OR ALBUMIN OR
                 GELATIN)
L60            4 SEA ABB=ON  PLU=ON  L58 AND BUFFER?
L61            1 SEA ABB=ON  PLU=ON  L60 AND (TEMP OR TEMPERATURE)
L62            0 SEA ABB=ON  PLU=ON  (L59 OR L61) NOT (L30 OR L36)

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN,
     TOXCENTER, PASCAL, FEDRIP, DISSABS' ENTERED AT 14:53:52 ON 27 OCT 2005
L63            4 SEA ABB=ON  PLU=ON  L59
L64            1 SEA ABB=ON  PLU=ON  L61
L65            0 SEA ABB=ON  PLU=ON  (L63 OR L64) NOT (L32 OR L44)

     FILE 'HOME' ENTERED AT 14:59:15 ON 27 OCT 2005


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   26 OCT 2005  HIGHEST RN 866186-08-5
     DICTIONARY FILE UPDATES:  26 OCT 2005  HIGHEST RN 866186-08-5

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************

     Structure search iteration limits have been increased.  See HELP SLIMI
     for details.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE HCAPLUS

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FILE COVERS 1907 - 27 Oct 2005 VOL 143 ISS 18
FILE LAST UPDATED: 26 Oct 2005 (20051026/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 26 OCT 2005 (20051026/UP). FILE COVERS 1950 TO DA

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 October 2005 (20051026/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 20 Oct 2005 (20051020/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 24 OCT 2005 <20051024/UP>
MOST RECENT DERWENT UPDATE: 200568 <200568/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

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>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
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>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code
FOR DETAILS. <<<

FILE JICST-EPLUS
FILE COVERS 1985 TO 24 OCT 2005 (20051024/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 4 OCT 2005 <20051004/UP>
FILE COVERS APR 1973 TO JUNE 30, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE PHIC
FILE COVERS CURRENT RECORDS AND IS UPDATED DAILY
FILE LAST UPDATED: 26 OCT 2005 (20051026/ED)

FILE PHIN
FILE COVERS 1980 TO 21 OCT 2005 (20051021/ED)

FILE TOXCENTER

FILE COVERS 1907 TO 25 Oct 2005 (20051025/ED)

This file contains CAS Registry Numbers for easy and accurate substanc identification.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TOXCENTER has been enhanced with new files segments and search fields. See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a description of changes.

FILE PASCAL
FILE LAST UPDATED: 24 OCT 2005 <20051024/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE

Searcher : Shears 571-272-2528

IN THE BASIC INDEX (/BI) FIELD <<<

FILE FEDRIP

FILE COVERS CURRENT DATA. LAST UPDATE: 16 SEP 2005 (20050916/ED)

FILE DISSABS
FILE COVERS 1861 TO 26 OCT 2005 (20051026/ED)

FILE CAPLUS

FILE COVERS 1907 - 27 Oct 2005 VOL 143 ISS 18
FILE LAST UPDATED: 26 Oct 2005 (20051026/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply
They are available for your review at:

http://www.cas.org/infopolicy.html

Searcher : Shears 571-272-2528

Devi, S.
09/393590

27oct05 13:21:47 User219783 Session D2121.2

SYSTEM:OS - DIALOG OneSearch
File 65:Inside Conferences 1993-2005/Oct W4
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File 440:Current Contents Search(R) 1990-2005/Oct 27
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File 348:EUROPEAN PATENTS 1978-2005/Oct W03
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File 357:Derwent Biotech Res. _1982-2005/Oct W5
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File 113:European R&D Database 1997
(c)1997 Reed-Elsevier(UK)Ltd All rts reserv
*File 113: This file is closed (no updates)

Set Items Description
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Set Items Description

- key terms

S2 10936 (BO OR BOTULIN?)(5N)(NT OR NEUROTOXIN? ? OR TOXIN? ? OR TOX??) OR BOTOX?? OR BONT?? OR BOTX?? OR BTX?? OR (BT OR BN OR BNT??)(10N)BOTULIN? OR BOTULIN?(3N)(A OR B OR C1 OR C2 OR D OR E OR F OR G)
S3 517116 PHOSPHATE OR SUCCINATE OR SUCCINIC OR ACETATE OR CITRATE OR BUTANEDIOIC OR ACETIC
S4 901 S2 AND S3
S5 335 S4 AND (NACL OR (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALINE)
S6 158 S5 AND (HSA(S)ALBUMIN OR SER??(W)ALBUMIN OR GELATIN? ?)
S7 146 S6 AND BUFFER?
S8 131 S7 AND (TEMP? ? OR TEMPERATURE? ?)
S9 125 S8 AND (PH OR (HYDROGEN OR H)(W)ION)
S10 7 S9 AND (CENTIGRADE OR CELSIUS)
S11 33 S9 AND ((UNIT? ? OR U)(2N)(ML OR MILLILIT? OR MILLI(W)(LITER? OR LITRE?)))
S12 39 S10 OR S11
S13 39 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

13/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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01967963
Compounds that block C5a complement receptor and their use in therapy
Substanzen die der C5a Komplementrezeptor blockieren und deren Verwendung in der Therapie
Composes qui bloquent le recepteur du complement C5a et leur utilisation en therapie
PATENT ASSIGNEE:
Alligator Bioscience AB (publ), (4453561), Scheelevagen 19a, 223 70 Lund, (SE), (Applicant designated States: all)
INVENTOR:
Van Strijp, Johannes, Antonius, Geradus, Singel 37, 3984 NV Odijk, (NL)
De Haas, Carla, Camminghalaan 12, 3981 GH Bunnik, (NL)
Kemmink, Johan, P.O. Box 80082, 3508 TB Utrecht, (NL)
Van Kessel, Kok, Kampweg 17, 3981 EX Bunnik, (NL)

Van Kessel, Kok, Kampweg 17, 3981 EX Bunnik, (NL)
LEGAL REPRESENTATIVE:
Thomas, Philip John Duval et al (76811), Eric Potter Clarkson, Park View House, 58 The Ropewalk, Nottingham NG1 5DD, (GB)
PATENT (CC, No, Kind, Date): EP 1586583 A2 051019 (Basic)
APPLICATION (CC, No, Date): EP 2004076120 040416;
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LI; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; HR; LT; LV; MK
INTERNATIONAL PATENT CLASS: C07K-014/31; A61K-038/16; G01N-033/566

ABSTRACT EP 1586583 A2
The present invention relates to compounds that are able to prevent intramolecular contact of the N-terminal residues 10 to 18 of human C5aR with the extracellular loops thereof. More specifically the invention relates to compounds that are able to bind the aspartates in positions 10, 15 and 18 and the glycine in position 12 of the human C5aR. Such compounds are preferably of the general formula Xn))-E-X39))-K-X7))-Y-V-X11))-Y-Xm)), wherein Xn)), X39)), X7)), X11)) and Xm)) are stretches of amino acids and the other letters represent the corresponding amino acids or non-proteinogenic analogs thereof. The invention further relates to their use in prophylaxis and therapy.
ABSTRACT WORD COUNT: 104
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200542	1875
SPEC A	(English)	200542	9283
Total word count - document A			11158
Total word count - document B			0
Total word count - documents A + B			11158

13/3,AB/2 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01949240
Globular assembly of amyloid beta protein and uses thereof
Globularer Aufbau vom Amyloid-beta- protein und deren Verwendungen
Assemblage de proteine amyloide beta globulaire et ses utilisations
PATENT ASSIGNEE:
THE UNIVERSITY OF SOUTHERN CALIFORNIA, (446674), University Park Los Angeles,, California 90089, (US), (Applicant designated States: all)
Northwestern University, (204952), 633 Clark Street Evanston, Illinois 60208, (US), (Applicant designated States: all)
INVENTOR:
Kraft, Grant A., 1309 Evergreen Court, Glenview, IL 60025, (US)
Klein, William L., 1145 Chatfield Road, Winnetka, IL 60093, (US)
Chromy, Brett A., 2004 Colfax Street, Evanston, IL 60201, (US)
Lambert, Mary P., 1956 Linneman Street, Glenview, IL 60025, (US)
Finch, Caleb E., 2144 Crescent Drive, Altadena, CA 91101, (US)
Morgan, Todd, 312 Fifteenth Place, Manhattan Beach, CA 90266, (US)
Wals, Pat, 11412 Pepper Lane, Nevada City, CA 90059-9686, (US)
Rozovsky, Irina, 2437 San Pasqual Street, Pasadena, CA 91107, (US)
Barlow, Ann, 2525 Noyes Street, Evanston, IL 60201, (US)

LEGAL REPRESENTATIVE:
Brown, John D. (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1571158 A2 050907 (Basic)
APPLICATION (CC, No, Date): EP 2004027742 000804;
PRIORITY (CC, No, Date): US 369236 990804
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK
RELATED PARENT NUMBER(S) - PN (AN):
EP 1200470 (EP 2000952571)
INTERNATIONAL PATENT CLASS: C07K-014/47; A61K-038/04; G01N-033/68

ABSTRACT EP 1571158 A2
The invention provides amyloid beta-derived dementing ligands (ADDLs) that comprise amyloid (beta) protein assembly bled into globular non-fibrillar oligomeric structures capable of activating specific cellular processes. The invention provides methods for assaying the formation, presence, receptor protein binding and cellular activity of ADDLs, as well as compounds that block the formation or activity of ADDLs, and methods of identifying such compounds. The invention further provides methods of using ADDLs, and modulating ADDL formation and/or activity, inter alia in the treatment of learning and/or memory disorders.
ABSTRACT WORD COUNT: 86
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200536	453
SPEC A	(English)	200536	24150
Total word count - document A			24603
Total word count - document B			0
Total word count - documents A + B			24603

13/3,AB/3 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01856099
Antisense modulation of BCL-X expression
Antisense Modulation der BCL-X Expression
Modulation antisens de l'expression du gene BCL-X
PATENT ASSIGNEE:
ISIS PHARMACEUTICALS, INC., (1382621), 2292 Faraday Avenue, Carlsbad, CA 92008, (US), (Applicant designated States: all)
INVENTOR:
Nickoloff, Brian J., 4 Turnberry Court, Burr Ridge, IL 60521-8396, (US)
Monia, Brett P., 2306 Casa Hermosa Court, Encinitas, CA 92024, (US)
Dean, Nicholas M., 2110 Whisperwind Lane, Olivenhain, CA 92024, (US)
Bennett, C. Frank, 1347 Cassins Street, Carlsbad, CA 92009, (US)
Zhang, QingQing, 5370 Ruette De Mer, San Diego, CA 92130, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53032), Carpmaels and Ransford, 43-45 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 1507005 A2 050216 (Basic)

EP 1507005 A3 050615
APPLICATION (CC, No, Date): EP 2004077688 990928;
PRIORITY (CC, No, Date): US 167921 981007; US 277020 990326; US 323743 990602
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 1119579 (EP 99949943)
INTERNATIONAL PATENT CLASS: C12N-015/11; C07H-021/04; C07H-021/02; A61K-048/00; C12N-015/85; C12N-015/86

ABSTRACT EP 1507005 A2
Compositions and methods are provided for modulating the expression of bcl-x. Antisense compounds, particularly antisense oligonucleotides, targeted to nucleic acids encoding bcl-x are preferred. Methods of using these compounds for modulation of bcl-x expression and for treatment of diseases associated with expression of bcl-x are also provided. Methods of sensitizing cells to apoptotic stimuli are also provided.
ABSTRACT WORD COUNT: 58

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200507	1492
SPEC A	(English)	200507	18182
Total word count - document A			19674
Total word count - document B			0
Total word count - documents A + B			19674

13/3,AB/4 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01843065
Preparation of fully human antibodies
Methoden zur Herstellung ganzlich humaner Antikorper.
Methodes pour la preparation des anticorps entierement humains
PATENT ASSIGNEE:
CCL Holdings Co., Ltd., (4931710), 8F, 163, Section 1 Ji-Long Road, Taipei, (TW), (Applicant designated States: all)
INVENTOR:
Chin, Li-Te, 9F-5, No.12, Lane 175, Wu-Ling Road, Hsin-Chu 300, (TW)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1498426 A1 050119 (Basic)
APPLICATION (CC, No, Date): EP 2004016838 040716;
PRIORITY (CC, No, Date): US 622003 030716
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LI; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; HR; LT; LV; MK
INTERNATIONAL PATENT CLASS: C07K-016/00; C12N-005/00; C07K-016/10

ABSTRACT EP 1498426 A1
The present invention provides a method of preparing fully human antibodies that recognize a pre-determined antigen without relying on human donors that have already been exposed to the antigen. To this end, lymphocytes from naive human donors are immunized in vitro with the antigen of interest, and cells that produce antibodies against the

antigen are identified. Since the lymphocytes are immunized in vitro rather than in vivo, it is possible to control which antigen, or which part of the antigen, would be recognized by the antibody. A preferred antigen is gp120 of HIV, particularly the co-receptor binding region of gp120.
ABSTRACT WORD COUNT: 101
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200503	882
SPEC A	(English)	200503	8412
Total word count - document A			9294
Total word count - document B			0
Total word count - documents A + B			9294

13/3,AB/5 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01801253
Affinity proteins for controlled application of cosmetic substances
Proteine mit hoher Affinitat fur kosmetische Substanzen mit gesteuerter Anwendung
Proteines a forte affinite pour des actives cosmetiques pour une application controlee
PATENT ASSIGNEE:
L-MAbs B.V., (4297560), Agro Business Park 40, 6708 PW Wageningen, (NL), (Applicant designated States: all)
INVENTOR:
Houtzager, Erwin, Koenestraat 13, 3958 XD Amerongen, (NL)
Vijn, Irma Maria Caecilia, Haldwerweg 105, 6721 ZJ Bennekom, (NL)
Sijmons, Peter Christiaan, Valeriusstraat 210-3, 1075 GK Amsterdam, (NL)
Mudge, Grant, 196 Lonetown Road, West Redding, Connecticut 06496, (US)
Fadel, Addi, 135 Long Hill Road, Shelton, Connecticut 06484, (US)
Valinotti, Tony, 4 Lester Road, Sandy Hook, Connecticut 06482, (US)
LEGAL REPRESENTATIVE:
Prins, Adrianus Willem, Mr. Ir. et al (20903), Vereenigde, Nieuwe Parklaan 97, 2587 BN Den Haag, (NL)
PATENT (CC, No, Kind, Date): EP 1470824 A1 041027 (Basic)
APPLICATION (CC, No, Date): EP 2002080206 021210;
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO
INTERNATIONAL PATENT CLASS: A61K-047/48; C07K-016/18

ABSTRACT EP 1470824 A1
Provided are means and methods for applying cosmetic substance to a desired target. The method comprising providing a conjugate of a proteinaceous substance having a specific affinity for said target molecule linked to a cosmetic substance, whereby the resulting connection between cosmetic substance and target molecule can be disrupted upon the presence of a chemical and/or physical signal.
ABSTRACT WORD COUNT: 59
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200444	919
SPEC A	(English)	200444	31252
Total word count - document A			32171
Total word count - document B			0
Total word count - documents A + B			32171

13/3,AB/6 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01779146
ADP-ribosyltransferase c3cer
ADP-Ribosyltransferase c3cer
ADP-ribosyltransferase c3cer
PATENT ASSIGNEE:
Migragen AG, (4151551), Spemannstrasse 34, 72076 Tubingen, (DE),
(Applicant designated States: all)
INVENTOR:
Aktories, Klaus, Prof. Dr. Dr., Ezmattenweg 22, 79189 Bad Krozingen, (DE)
Wilde, Christian, Dr., Kandelstrasse 44, 79106 Freiburg, (DE)
LEGAL REPRESENTATIVE:
Bosl, Raphael, Dr.rer.nat., Dipl.-Chem. (74947), Patentanwalte Isenbruck
Bosl Horschler Wichmann Huhn Prinzregentenstrasse 68, 81675 Munchen,
(DE)
PATENT (CC, No, Kind, Date): EP 1452589 A1 040901 (Basic)
EP 1452589 A1 040901
APPLICATION (CC, No, Date): EP 2003004346 030228;
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR;
HU; IE; IT; LI; LU; MC; NL; PT; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO
INTERNATIONAL PATENT CLASS: C12N-009/10; C12N-015/62; C12N-015/54;
C12N-005/10; A61K-038/45; C07K-014/21

ABSTRACT EP 1452589 A1
The present invention relates to the ADP-Ribosyltransferase C3cer and its use for the preparation of a pharmaceutical composition for the regeneration of neurons and/or the stimulation of the growth of neurons.
ABSTRACT WORD COUNT: 32
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200436	770
SPEC A	(English)	200436	6930
Total word count - document A			7700
Total word count - document B			0
Total word count - documents A + B			7700

13/3,AB/7 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01674389
Transgenic and cloned mammals
Transgen- und klonierte Saugentiere
Mammiferes trangeniques et clones
PATENT ASSIGNEE:
GTC Biotherapeutics, Inc., (4312522), 175 Crossing Boulevard,, Framingham, MA 01702, (US), (Applicant designated States: all)
INVENTOR:
Echelard, Yann, 248 Moss Hill Road, Jamaica Plains, MA 02131, (US)
LEGAL REPRESENTATIVE:
Ruffles, Graham Keith (43043), Marks & Clerk, 66-68 Hills Road, Cambridge, Cambridgeshire CB2 1LA, (GB)
PATENT (CC, No, Kind, Date): EP 1375654 A2 040102 (Basic)
APPLICATION (CC, No, Date): EP 2003014030 991102;
PRIORITY (CC, No, Date): US 106728 981102; US 298508 990422; US 298971 990423; US 131328 990426
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 1127113 (EP 99971451)
INTERNATIONAL PATENT CLASS: C12N-015/00; A01K-067/027; C07K-014/81

ABSTRACT EP 1375654 A2
The invention features methods of making cloned and transgenic non-human mammals, for instance goats. The methods include making a somatic cell line, for instance a transgenic somatic cell line, which can be used as a donor cell, methods of producing a cloned or transgenic non-human mammal by introducing the genome of a somatic cell into an enucleated oocyte, preferably a naturally matured oocyte in the metaphase II stage of meiotic cell division, to form a reconstructed embryo, and methods of transferring the reconstructed embryo. The invention also includes cell lines, reconstructed embryos and cloned or transgenic non-human mammals.
ABSTRACT WORD COUNT: 99

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200401	635
SPEC A	(English)	200401	25452
Total word count - document A			26087
Total word count - document B			0
Total word count - documents A + B			26087

13/3,AB/8 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01663911
Genetically engineered vaccine strain
Gentechnologisch hergestellter Stamm fur Impfstoffe
Souche de vaccin mise au point par genie genetique
PATENT ASSIGNEE:
Connaught Technology Corporation, (4514650), 3711 Kennett Pike, Suite 200 , Greenville, DE 19807, (US), (Applicant designated States: all)
INVENTOR:
Paoletti, Enzo, 297 Murray Avenue, Delmar, NY 12054, (US)

Perkus, Marion E., Box 276A, RD No. 2, 4971 Western Turnpike, Altamont, NY 12009, (US)
Taylor, Jill, 22 Rose Court, Albany, NY 12209, (US)
Tartaglia, James, 7 Christina Drive, Schenectady, NY 12303, (US)
Norton, Elizabeth K., 14 Surrey Hill Drive, Latham, NY 12110, (US)
Riviere, Michel, 11 Chemin du Chancellier, 69130 Ecully, (FR)
De Taisne, Charles, 410 Manning Boulevard, Albany, NY 12206, (US)
Limbach, Keith J., 12353 Morning Light Terrace, Gaitherburg, MD 20878, (US)
Johnson, Gerard P., 100 Devitt Road, Waterford, NY 12188, (US)
Pincus, Steven E., 78 Troy Road, East Greenbush, NY 12061, (US)
Cox, William I., 1 Washington Place, Troy, NY 12180, (US)
Audonnet, Jean-Christophe Francis, 596 Warren Street No. 6, Albany, NY 12201, (US)
Gettig, Russell Gilbert, R.D. 2, Box 421 C, Averill Park, NY 12018, (US)
LEGAL REPRESENTATIVE:
Mallalieu, Catherine Louise et al (69621), D. Young & Co., 21 New Fetter Lane, London EC4A 1DA, (GB)
PATENT (CC, No, Kind, Date): EP 1367128 A1 031203 (Basic)
APPLICATION (CC, No, Date): EP 2003018214 920309;
PRIORITY (CC, No, Date): US 666056 910307; US 713967 910611; US 847951 920306
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 575491 (EP 92908110)
INTERNATIONAL PATENT CLASS: C12N-015/863; C12N-007/00; C12N-015/00; C12P-021/06; A61K-039/12

ABSTRACT EP 1367128 A1
What is described is a modified vector, such as a recombinant poxvirus, particularly recombinant vaccina virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulance. In one embodiment, the genetic functions are inactivated by deleting an open reading frame encoding a virulence factor. In another embodiment, the genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus vaccines.
ABSTRACT WORD COUNT: 110
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200349	738
SPEC A	(English)	200349	103084
Total word count - document A			103822
Total word count - document B			0
Total word count - documents A + B			103822

13/3,AB/9 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01616603
Therapeutic use of non-neurotoxic clostridium **botulinum toxin** type **C2**
Therapeutische Verwendung des nicht-neurotoxischen Clostridium **Botulinum Toxins** Typ **C2**
Utilisation therapeutique de non-neurotoxic **botulinum** clostridium **toxine** type **C2**
PATENT ASSIGNEE:
Botulinum Toxin Research Associates, Inc., (4042650), 1261 Furnace Brook Parkway, Quincy, Massachusetts 02169, (US), (Applicant designated States: all
INVENTOR:
Borodic, Gary E., 90 Kensington Drive, Canton, Massachusetts 02021, (US)
LEGAL REPRESENTATIVE:
Gardner, Rebecca (90041), Frank B. Dehn & Co. 179 Queen Victoria Street, London EC4V 4EL, (GB)
PATENT (CC, No, Kind, Date): EP 1334729 A1 030813 (Basic)
APPLICATION (CC, No, Date): EP 2002250834 020207;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-038/45; C12N-009/10; A61P-037/00; A61P-027/00; A61P-021/00

ABSTRACT EP 1334729 A1
The invention relates to clostridial toxin compositions and their use for the treatment of diseases, particularly diseases which are associated with pain, inflammation and irritation, as well as movement disorders. In particular, the invention provides **a botulinum toxin** which substantially lacks neurotoxic activity, or a biologically active component thereof which substantially lacks neurotoxic activity, for use in therapy.
ABSTRACT WORD COUNT: 59
NOTE:
Figure number on first page: 2

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200333	713
SPEC A	(English)	200333	6857
Total word count - document A			7570
Total word count - document B			0
Total word count - documents A + B			7570

13/3,AB/10 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01586625
TAILOR-MADE MULTIFUNCTIONAL STEM CELLS AND UTILIZATION THEREOF
GEZIELT HERGESTELLTE MULTIFUNKTIONELLE STAMMZELLEN UND IHRE VERWENDUNG
CELLULES SOUCHES MULTIFONCTIONNELLES ADAPTEES ET UTILISATION DE CES DERNIERES
PATENT ASSIGNEE:
ReproCELL Inc., (4629280), The Imperial Tower Hotel 12F, 1-1-1 Uchisaiwaicho, Chiyoda-ku, Tokyo 100-0011, (JP), (Applicant designated

States: all)
Nakatsuji, Norio, (4399760), 273-7, Iwakuranishigawaracho, Sakyo-ku, Kyoto-shi, Kyoto 606-0014, (JP), (Applicant designated States: all)
Tada, Takashi, (4399780), 49-10, Yoshidashimoojicho, Sakyo-ku, Kyoto-shi, Kyoto 606-8314, (JP), (Applicant designated States: all)
INVENTOR:
NAKATSUJI, Norio, 273-7, Iwakuranishigawaracho, Sakyo-ku, Kyoto-shi, Kyoto 606-0014, (JP)
TADA, Takashi, 49-10, Yoshidashimoojicho, Sakyo-ku, Kyoto-shi, Kyoto 606-8314, (JP)
TADA, Masako, 49-10, Yoshidashimoojicho, Sakyo-ku, Kyoto-shi, Kyoto 606-8314, (JP)
LEGAL REPRESENTATIVE:
Holliday, Louise Caroline (95451), D Young & Co, 21 New Fetter Lane, London EC4A 1DA, (GB)
PATENT (CC, No, Kind, Date): EP 1437404 A1 040714 (Basic)
WO 2003027278 030403
APPLICATION (CC, No, Date): EP 2002799492 020920; WO 2002JP9732 020920
PRIORITY (CC, No, Date): JP 2001290005 010921
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/02; C12N-005/06; C12N-009/10; C12Q-001/02; A61L-027/38; A61K-045/00; A61K-048/00

ABSTRACT EP 1437404 A1
An object of the present invention is to efficiently establish cells, tissues, and organs capable of serving as donors for treating diseases, without eliciting immune rejection reactions, without starting with an egg cell. This object was achieved by providing a pluripotent stem cell having a desired genome. The cell was produced by treating with a reprogramming agent, producing a fusion cell of an MHC deficient stem cell with a somatic cell, or after producing a fusion cell of a stem cell with a somatic cell, removing a gene derived from the stem cell by performing genetic manipulation with a retrovirus.
ABSTRACT WORD COUNT: 101
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200429	1269
SPEC A	(English)	200429	30554
Total word count - document A			31823
Total word count - document B			0
Total word count - documents A + B			31823

13/3,AB/11 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01468215
CELL PROLIFERATION INHIBITORS COMPRISING ETS TRANSCRIPTION FACTOR OR GENE ENCODING THE SAME
ZELLPROLIFERATIONSHEMMER MIT ETS-TRANSKRIPTIONSFAKTOR ODER DAFUR KODIERENDES GEN
INHIBITEURS DE LA PROLIFERATION CELLULAIRE COMPRENANT UN FACTEUR DE

TRANSCRIPTION ETS OU UN GENE CODANT CE DERNIER
PATENT ASSIGNEE:
HISAMITSU PHARMACEUTICAL CO. INC., (444623), 408, Tashirodaikanmachi, Tosu-shi, Saga-ken 841-0017, (JP), (Applicant designated States: all)
INVENTOR:
KAI, Hirofumi, 3-10-30, Kokubu, Kumamoto-shi, Kumamoto 862-0949, (JP)
HISATSUNE, Akinori, c/o HISAMITSU PHARMA. CO. INC., 25-11, Kannondai 1-chome, Tsukuba-shi, Ibaraki 305-0856, (JP)
LEGAL REPRESENTATIVE:
Cresswell, Thomas Anthony et al (50351), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 1366773 A1 031203 (Basic)
EP 1366773 A8 050727
WO 2002064165 020822
APPLICATION (CC, No, Date): EP 2002712308 020213; WO 2002JP1180 020213
PRIORITY (CC, No, Date): JP 200134834 010213
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-045/00; A61K-038/17; A61K-031/711; A61K-048/00; A61P-043/00; A61P-035/00; A61P-029/00; G01N-033/15; G01N-033/50

ABSTRACT EP 1366773 A1
It is found out that an ETS transcription factor (more specifically, an ETS transcription factor MEF) has a potent effect of inhibiting cell proliferation and an effect of inhibiting MMP production. Based on this finding, novel cell proliferation inhibitors (more specifically, novel remedies for tumor and novel antirheumatics) with the use of the ETS transcription factor MEF or a gene encoding the same are provided. Namely, cell proliferation inhibitors comprising an ETS transcription factor or gene encoding the same or a substance controlling the effect of the ETS transcription factor or the gene encoding the same. Also, matrix metalloprotease (MMP) (more specifically, MMP-9) production inhibitors or IL-8 production inhibitors comprising the ETS transcription factor or gene encoding the same or a substance controlling the effect of the ETS transcription factor or the gene encoding the same are provided.
ABSTRACT WORD COUNT: 139
NOTE:
Figure number on first page: 10

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200349	671
SPEC A	(English)	200349	14067
Total word count - document A			14738
Total word count - document B			0
Total word count - documents A + B			14738

13/3,AB/12 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01421490
METHOD OF AMPLIFYING NUCLEIC ACID
VERFAHREN ZUR VERVIELFALTIGUNG VON NUKLEINSAUREN
PROCEDE D'AMPLIFICATION D'ACIDE NUCLEIQUE

PATENT ASSIGNEE:
TAKARA BIO INC., (4118471), 4-1, Seta 3-chome, Otsu-shi, Shiga 520-2193, (JP), (Applicant designated States: all)
INVENTOR:
SAGAWA, Hiroaki, 6-32, Nishishibukawa 2-chome, Kusatsu-shi, Shiga 525-0025, (JP)
UEMORI, Takashi, 709, Sharumankopo-daini-seta, 1-16, Oe 3-chome, Otsu-shi, Shiga 520-2141, (JP)
MUKAI, Hiroyuki, 1461-82, Aza Minamikawa, Mizuho-cho, Moriyama-shi, Shiga 524-0102, (JP)
YAMAMOTO, Junko, 332-2, Furutaka-cho, Moriyama-shi, Shiga 524-0044, (JP)
TOMONO, Jun;, 313, Hamoparesu-Kusatsu, 2-12-1, Nishishibukawa, Kusatsu-shi, Shiga 525-0025, (JP)
KOBAYASHI, Eiji, 18-19, Ichiriyama 6-chome, Otsu-shi, Shiga 520-2153, (JP)
ENOKI, Tatsuji, 202, Inouehausu, 10-23, Nango 1-chome, Otsu-shi, Shiga 520-0865, (JP)
ASADA, Kiyozo, 3-20-9, Kibogaoka, Konan-cho, Koka-gun, Shiga 520-3333, (JP)
KATO, Ikunoshin, 1-1-150, Nanryo-cho, Uji-shi, Kyoto 611-0028, (JP)
LEGAL REPRESENTATIVE:
Grund, Martin, Dr. et al (90762), Dr. Volker Vossius Patentanwaltskanzlei Geibelstrasse 6, 81679 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1312682 A1 030521 (Basic)
WO 2002016639 020228
APPLICATION (CC, No, Date): EP 2001956988 010821; WO 2001JP7139 010821
PRIORITY (CC, No, Date): JP 2000251981 000823; JP 2000284419 000919; JP 2000288750 000922; JP 2001104191 010403
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12Q-001/68; C12N-015/09

ABSTRACT EP 1312682 A1
A method of highly sensitively and specifically amplifying a target nucleic acid in a sample by using a chimeric oligonucleotide primer having a ribonucleotide provided at the 3'-terminus or in the 3'-terminal side, an endoribonuclease and a DNA polymerase having a chain transfer activity, i.e., an isothermal and chimeric primer-initiated amplification of nucleic acids (ICAN) method; a method of detecting an amplified fragment obtained by using the above method; a process for producing a target nucleic acid by using the above amplification method; and chimeric oligonucleotide primers to be used in these methods.
ABSTRACT WORD COUNT: 94
NOTE:
Figure number on first page: 0035

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200321	5981
SPEC A	(English)	200321	57025
Total word count - document A			63006
Total word count - document B			0
Total word count - documents A + B			63006

13/3,AB/13 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01394688
PROCESS FOR PRODUCING PLANT-ORIGIN ANTIBACTERIAL SUBSTANCE
VERFAHREN ZUR HERSTELLUNG EINER AUS PFLANZEN STAMMENDEN, ANTIBAKTERIELLEN SUBSTANZ
PROCEDE DE PRODUCTION D'UNE SUBSTANCE ANTIBACTERIENNE D'ORIGINE VEGETALE
PATENT ASSIGNEE:
SAKAI, Takuo, (315581), 4-13-6, Harayamadai, Sakai-shi Osaka 590-0132, (JP), (Proprietor designated states: all)
INVENTOR:
SAKAI, Takuo, 4-13-6, Harayamadai, Sakai-shi Osaka 590-0132, (JP)
LEGAL REPRESENTATIVE:
Doireau, Marc (44325), Cabinet ORES, 36,rue de St Petersbourg, 75008 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 1209238 A1 020529 (Basic)
EP 1209238 B1 051019
WO 2001098519 011227
APPLICATION (CC, No, Date): EP 2001936956 010611; WO 2001JP4929 010611
PRIORITY (CC, No, Date): JP 2000189614 000623
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12P-001/00; A01N-065/00

ABSTRACT EP 1209238 A1
A process for producing an antibacterial substance which comprises disintegrating at least a part of a plant tissue and releasing the antibacterial substance therefrom; and antibacterial or bacteriostatic compositions containing the antibacterial substance thus obtained as the active ingredient. By using the above process and compositions, the proliferation of spore-forming bacteria can be efficiently inhibited.
ABSTRACT WORD COUNT: 56
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200222	227
CLAIMS B	(English)	200542	197
CLAIMS B	(German)	200542	191
CLAIMS B	(French)	200542	218
SPEC A	(English)	200222	2848
SPEC B	(English)	200542	2994
Total word count - document A			3076
Total word count - document B			3600
Total word count - documents A + B			6676

13/3,AB/14 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01352431
Matrix protein compositions for inflammatory and infectious conditions
Matrixprotein enthaltende Zusammensetzungen fur entzundliche und infektiose Zustande
Compositions proteiniques matricielles pour des conditions inflammatoires

et infectieuses
PATENT ASSIGNEE:
Biora Bioex AB, (1401681), Per Albin Hanssons Vag 41, 205 12 Malmo, (SE), (Proprietor designated states: all)
INVENTOR:
Gestrelius, Stina, St. Sgridsgatan 5, 223 50 Lund, (SE)
Hammarstrom, Lars, Frejavagen 28, 182 64 Djursholm, (SE)
Lyngstadaas, Staele Peter, Haakons vei 5, 1450 Nesoddtangen, (NO)
Andersson, Christer, Vellinge 27:12, 235 91 Vellinge, (SE)
Slaby, Ivan, Ingenjorsgatan, 03,, 215 68 - Malmo, (SE)
Hammargren, Tomas, Sanekullavagen 18, 217 74 Malmo, (SE)
LEGAL REPRESENTATIVE:
Dahner, Christer et al (87303), Strom & Gulliksson IP AB, Box 7086, 103 87 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 1153610 A1 011114 (Basic)
EP 1153610 B1 030820
APPLICATION (CC, No, Date): EP 2001201915 990226;
PRIORITY (CC, No, Date): DK 98270 980227; US 81551 P 980413; DK 981328 981016
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 1059934 (EP 99903852)
INTERNATIONAL PATENT CLASS: A61K-038/39; A61P-031/00; A61P-029/00

ABSTRACT EP 1153610 A1
Active enamel substances may be used for the preparation of a pharmaceutical or cosmetic composition for healing of a wound, improving healing of a wound, soft tissue regeneration or repair, or for preventing or treating infection or inflammation.
ABSTRACT WORD COUNT: 39
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200146	233
CLAIMS B	(English)	200334	233
CLAIMS B	(German)	200334	214
CLAIMS B	(French)	200334	249
SPEC A	(English)	200146	19381
SPEC B	(English)	200334	18864
Total word count - document A			19617
Total word count - document B			19560
Total word count - documents A + B			39177

13/3,AB/15 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01324561
Mammalian osteoregulins
Saugetier Osteoreguline
Osteoregulines mammiferes
PATENT ASSIGNEE:
Pfizer Products Inc., (2434221), Eastern Point Road, Groton, Connecticut

06340, (US), (Applicant designated States: all)
INVENTOR:
Brown, Thomas Aquinas, Pfizer Global Res. and Dev., Eastern Point Road, Groton, Connecticut 06340, (US)
De Wet, Jeffrey Roux, Pfizer Global Res. and Dev., Eastern Point Road, Groton, Connecticut 06340, (US)
Gowen, Lori Christine, 310 East 66th Street, Apartment 4D, New York 10021, (US)
Hames, Lynn Marie, Pfizer Global Res. and Dev., Eastern Point Road, Groton, Connecticut 06340, (US)
LEGAL REPRESENTATIVE:
Hayles, James Richard et al (75142), Pfizer Limited, Patents Department, Ramsgate Road, Sandwich Kent CT13 9NJ, (GB)
PATENT (CC, No, Kind, Date): EP 1130098 A2 010905 (Basic)
EP 1130098 A3 030910
APPLICATION (CC, No, Date): EP 2001301768 010227;
PRIORITY (CC, No, Date): US 185617 P 000229; US 234500 P 000922
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/47; A01K-067/027; C12Q-001/68; G01N-033/68

ABSTRACT EP 1130098 A2
The invention features novel osteoregulin polypeptides, nucleic acid sequences which encode the polypeptides, vectors, antibodies, hosts which express heterologous osteoregulins, and animal cells and mammals with a targeted disruption of an osteoregulin gene. These osteoregulins play a role in regulating bone homeostasis, adiposity, and the calcification of atherosclerotic plaques. Accordingly, the invention also features screening assays to identify modulators of osteoregulin activity as well as methods of treating mammals for diseases or disorders associated with osteoregulin activity.
ABSTRACT WORD COUNT: 79
NOTE:
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200136	898
SPEC A	(English)	200136	28794
Total word count - document A			29692
Total word count - document B			0
Total word count - documents A + B			29692

13/3,AB/16 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01266016
GLOBULAR ASSEMBLY OF AMYLOID BETA PROTEIN AND USES THEREOF
GLOBULARER AUFBAU VOM AMYLOID-BETA- PROTEIN UND DEREN VERWENDUNGEN
ASSEMBLAGE DE PROTEINE AMYLOIDE B GLOBULAIRE ET SES UTILISATIONS
PATENT ASSIGNEE:
THE UNIVERSITY OF SOUTHERN CALIFORNIA, (446674), University Park, Los Angeles, California 90089, (US), (Proprietor designated states: all)
NORTHWESTERN UNIVERSITY, (204952), 633 Clark Street, Evanston Illinois 60208, (US), (Proprietor designated states: all)

INVENTOR:
KRAFFT, Grant, A., 1309 Evergreen Court, Glenview, IL 60025, (US)
KLEIN, William, L., 1145 Chatfield Road, Winnetka, IL 60093, (US)
CHROMY, Brett, A., 2004 Colfax Street, Evanston, IL 60201, (US)
LAMBERT, Mary, P., 1956 Linneman Street, Glenview, IL 60025, (US)
FINCH, Caleb, E., 2144 Crescent Drive, Altadena, CA 91101, (US)
MORGAN, Todd, 312 Fifteenth Place, Manhattan Beach, CA 90266, (US)
WALS, Pat, 924 Elyria Drive, Los Angeles, Ca 90065, (US)
ROZOVSKY, Irina, 2437 San Pasqual Street, Pasadena, CA 91107, (US)
BARLOW, Ann, 2525 Noyes Street, Evanston, IL 60201, (US)
LEGAL REPRESENTATIVE:
Brown, John David (28811), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1200470 A2 020502 (Basic)
EP 1200470 B1 041124
WO 2001010900 010215
APPLICATION (CC, No, Date): EP 2000952571 000804; WO 2000US21458 000804
PRIORITY (CC, No, Date): US 369236 990804
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2004027742)
INTERNATIONAL PATENT CLASS: C07K-014/47; G01N-033/68; A61K-038/04
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200448	2233
CLAIMS B	(German)	200448	2174
CLAIMS B	(French)	200448	2474
SPEC B	(English)	200448	21046
Total word count - document A			0
Total word count - document B			27927
Total word count - documents A + B			27927

13/3,AB/17 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01196162
Vaccine and antitoxin for treatment and prevention of C. difficile disease
Impfstoff und Antitoxine zur Behandlung und Vorbeugung von C. Difficile Krankheiten
Vaccin et antitoxines pour le traitement et la prevention de maladies causees par C. difficile
PATENT ASSIGNEE:
OPHIDIAN PHARMACEUTICALS, INC., (1819051), 5445 East Cheryl Parkway, Madison, WI 53711, (US), (Applicant designated States: all)
INVENTOR:
Williams, James A., 6420 Pueblo Court, Lincoln, NE 68516, (US)
Padhye, Nisha V., 4535 Birchhollow Drive, Lincoln, NE 68516, (US)
Thalley, Bruce S., 925 High Street. no. 2, Madison, WI 53719, (US)
Stafford, Douglas C., 5743 Timer View Court, Madison, WI 53711, (US)
Firca, Joseph R., 123 Deerpath Drive, Vernon Hills, IL 60061, (US)
Kink, John A., 110 Wolf Street, Madison, WI 53717, (US)
LEGAL REPRESENTATIVE:

Glawe, Delfs, Moll & Partner (100691), Patentanwalte Rothenbaumchaussee 58, 20148 Hamburg, (DE)
PATENT (CC, No, Kind, Date): EP 1041149 A2 001004 (Basic)
EP 1041149 A3 010502
APPLICATION (CC, No, Date): EP 105371 951023;
PRIORITY (CC, No, Date): US 329154 941024; US 405496 950316; US 422711 950414; US 480604 950607
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 796326 (EP 95937626)
INTERNATIONAL PATENT CLASS: C12N-015/31; C12N-001/21; C07K-014/33; C07K-016/12; C07K-001/22; A61K-038/16; A61K-039/08; C12R-1:145

ABSTRACT EP 1041149 A2
The present invention provides neutralizing antitoxin directed against C.difficile toxins. These antitoxins are produced in avian species using soluble recombinant C.difficile toxin proteins. The avian antitoxins are designed so as to be orally administrable in therapeutic amounts and may be in any form (i.e., as a solid or in aqueous solution). Solid forms of the antitoxin may comprise an enteric coating. These antitoxins are useful in the treatment of humans and other animals intoxicated with at least one bacterial toxin. The invention further provides vaccines capable of protecting a vaccinated recipient from the morbidity and mortality associated with C.difficile infection. These vaccines are useful for administration to humans and other animals at risk of exposure to C.difficile toxins.
ABSTRACT WORD COUNT: 119
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200040	869
SPEC A	(English)	200040	95603
Total word count - document A			96472
Total word count - document B			0
Total word count - documents A + B			96472

13/3,AB/18 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01172621
High-throughput screening of gene function using libraries for functional genomics applications
Effizientes Verfahren zum Auffinden von Genfunktionen mittels Bibliotheken zur funktionellen Genomanwendung
Procede de criblage a fort rendement de la fonction d'un gene en utilisant des bibliotheques pour analyses fonctionelles de genomes
PATENT ASSIGNEE:
Galapagos Genomics N.V., (3370130), Generaal de Wittelaan 11 A3, 2800 Mechelen, (BE), (Proprietor designated states: all)
INVENTOR:
Schouten, Govert, Da Costastraat 82, 2321 AR Leiden, (NL)
Vogels, Ronald, van Rietlaan 4, 3461 HW Linschoten, (NL)

Bout, Abraham, Coymansstraat 24, 2751 AR Moerkapelle, (NL)
van Es, Helmuth, Bandholm 89, 2133 DJ Hoofddorp, (NL)
LEGAL REPRESENTATIVE:
Prins, Hendrik Willem et al (55081), Arnold & Siedsma, Advocaten en Octrooigemachtigden, Sweelinckplein 1, 2517 GK Den Haag, (NL)
PATENT (CC, No, Kind, Date): EP 1022335 A1 000726 (Basic)
EP 1022335 B1 040331
APPLICATION (CC, No, Date): EP 99201866 990611;
PRIORITY (CC, No, Date): US 97239 980612
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/10; C12N-015/86; C12N-005/10

ABSTRACT EP 1022335 A1
Novel means and methods for their use are provided to determine the function of the product(s) of one or more sample nucleic acids. The sample nucleic acids are synthetic oligonucleotides, DNA, or cDNA and encode polypeptides, antisense nucleic acids or GSEs. The sample nucleic acids are expressed in a host by a vehicle to alter at least one phenotype of the host. The altered phenotype(s) is identified as a means to assign a biological function to the product(s) encoded by the sample nucleic acid(s).
ABSTRACT WORD COUNT: 85
NOTE:
Figure number on first page: 36II

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200030	973
CLAIMS B	(English)	200414	1273
CLAIMS B	(German)	200414	1157
CLAIMS B	(French)	200414	1330
SPEC A	(English)	200030	37684
SPEC B	(English)	200414	38916
Total word count - document A			38664
Total word count - document B			42676
Total word count - documents A + B			81340

13/3,AB/19 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01149591
STABLE LIQUID FORMULATIONS OF BOTULINUM TOXIN
STABILISIERTE FLUSSIGE ARZNEIZUBEREITUNGEN ENTHALTEND **BOTULINUM TOXIN**
FORMULATIONS LIQUIDES STABLES DE LA **TOXINE** DE **BOTULINUM**
PATENT ASSIGNEE:
Elan Pharmaceuticals, Inc., (2709860), 800 Gateway Boulevard, South San Francisco, CA 94080, (US), (Proprietor designated states: all)
INVENTOR:
MOYER, Elizabeth, 435 Marin Avenue, Mill Valley, CA 94941, (US)
HIRTZER, Pamela, 291 Scenic Avenue, Piedmont, CA 94611, (US)
LEGAL REPRESENTATIVE:
Lee, Nicholas John et al (76842), Kilburn & Strode, 20 Red Lion Street, London WC1R 4PJ, (GB)

PATENT (CC, No, Kind, Date): EP 1112082 A2 010704 (Basic)
EP 1112082 B1 020731
WO 200015245 000323
APPLICATION (CC, No, Date): EP 99945649 990909; WO 99US20912 990909
PRIORITY (CC, No, Date): US 99870 P 980911
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-038/16; A61K-047/02; A61K-047/12; A61P-021/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200231	671
CLAIMS B	(German)	200231	645
CLAIMS B	(French)	200231	771
SPEC B	(English)	200231	9547
Total word count - document A			0
Total word count - document B			11634
Total word count - documents A + B			11634

13/3,AB/20 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01134551
Anti-Fas Antibodies
Anti-Fas-Antikorper
Anticorps anti-Fas
PATENT ASSIGNEE:
Sankyo Company Limited, (204886), 5-1, Nihonbashi-Honcho 3-chome, Chuo-ku, Tokyo 103-8426, (JP), (Applicant designated States: all)
INVENTOR:
Serizawa, Nobufasa, c/o Sankyo Co. Ltd., 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, (JP)
Haruyama, Hideyuki, c/o Sankyo Co. Ltd., 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, (JP)
Nakahara, Kaori, c/o Sankyo Co. Ltd., 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, (JP)
Tamaki, Ikuko, c/o Sankyo Co. Ltd., 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, (JP)
Takahashi, Tohru, c/o Sankyo Co. Ltd., 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, (JP)
LEGAL REPRESENTATIVE:
Gibson, Christian John Robert et al (30951), MARKS & CLERK, 57/60 Lincoln's Inn Fields, London WC2A 3LS, (GB)
PATENT (CC, No, Kind, Date): EP 990663 A2 000405 (Basic)
EP 990663 A3 020417
APPLICATION (CC, No, Date): EP 99307711 990929;
PRIORITY (CC, No, Date): JP 98276881 980930; JP 98276882 980930
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C07K-016/28; C12N-015/13; C12N-015/62; C12N-015/70; C12N-001/21; A61K-039/395

ABSTRACT EP 990663 A2
Anti-Fas antibodies are cross-reactive with mouse and human Fas and are useful in the treatment of conditions attributable to abnormalities in the Fas/Fas ligand system.
ABSTRACT WORD COUNT: 26
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200014	1483
SPEC A	(English)	200014	58480
Total word count - document A			59963
Total word count - document B			0
Total word count - documents A + B			59963

13/3,AB/21 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01036583
METHODS OF USE AND COMPOSITIONS FOR BENZYLIDENE- AND CINNAMYLIDENE-ANABASEINES
BENZYLIDENE- UND CINNAMYLIDENE-ANABASEINE ALS NEURONALE NIKOTIN ALPHA-7 REZEPTORAGONISTEN
PROCEDES D'UTILISATION ET COMPOSITIONS DE BENZYLIDENE-ANABASINES ET CINNAMYLIDENE-ANABASINES
PATENT ASSIGNEE:
University of Florida, (2395911), P.O. Box 115500, Gainesville, FL 32611-5500, (US), (Proprietor designated states: all)
INVENTOR:
MEYER, Edwin, 6101 N.W. 23rd Terrace, Gainesville, FL 32606, (US)
KEM, William, R., 1809 N.W. 47th Street, Gainesville, FL 32605, (US)
VAN HAAREN, Frans, 3807 N.W. 54th Way, Gainesville, FL 32653, (US)
ZOLTEWICZ, John, A., 2330 N.W. 38th Street, Gainesville, FL 32605, (US)
DEFIEBRE, Christopher, M., 7201 Mesa Verde Trail, Fort Worth, TX 76137, (US)
PAPKE, Roger, 2521 N.W. 63rd Terrace, Gainesville, FL 32606, (US)
DAY, Arthur, L., 2300 N.W. 29th Street, Gainesville, FL 32605, (US)
LEGAL REPRESENTATIVE:
Glawe, Delfs, Moll & Partner (100691), Patentanwalte Rothenbaumchaussee 58, 20148 Hamburg, (DE)
PATENT (CC, No, Kind, Date): EP 1045842 A2 001025 (Basic)
EP 1045842 B1 030514
WO 99010338 990304
APPLICATION (CC, No, Date): EP 98944579 980828; WO 98US17850 980828
PRIORITY (CC, No, Date): US 924008 970829
DESIGNATED STATES: DE; FR; GB; IT; NL
INTERNATIONAL PATENT CLASS: C07D-401/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200320	955
CLAIMS B	(German)	200320	926
CLAIMS B	(French)	200320	1101

SPEC B (English) 200320 15552
Total word count - document A 0
Total word count - document B 18534
Total word count - documents A + B 18534

13/3,AB/22 (Item 22 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01015139
Anti-fas antibodies
Antikorper gegen Fas
Anticorps contre Fas
PATENT ASSIGNEE:
Sankyo Company Limited, (204886), 5-1, Nihonbashi-Honcho 3-chome, Chuo-ku, Tokyo 103-8426, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Serizawa, Nobufusa, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Ichikawa, Kimihisa, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Ohsumi, Jun, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Ohtsuki, Masahiko, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Haruyama, Hideyuki, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Takahashi, Tohru, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Yoshida, Hiroko, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Shiraishi, Akio, Sankyo Company Limited, 2-58, Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, (JP)
Yonehara, Shin, 9-5, Matsuoido-cho, Nishikyo-ku, Kyoto-shi, Kyoto-fu, (JP)
LEGAL REPRESENTATIVE:
Gibson, Christian John Robert (30951), MARKS & CLERK, 57/60 Lincoln's Inn Fields, London WC2A 3LS, (GB)
PATENT (CC, No, Kind, Date): EP 909816 A1 990421 (Basic)
APPLICATION (CC, No, Date): EP 98302575 980401;
PRIORITY (CC, No, Date): JP 9782953 970401; JP 97169088 970625; JP 97276064 971008
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/13; C07K-016/28; C07K-014/705; C07K-016/46; C12N-015/62; C12N-015/70; C12N-001/21; A61K-039/395; C12N-005/20; C12N-015/06;

ABSTRACT EP 909816 A1
Anti-human Fas antibodies which are cross-reactive with mouse and human Fas are useful in the treatment of conditions attributable to abnormalities in the Fas/Fas ligand system.
ABSTRACT WORD COUNT: 27

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count

CLAIMS A	(English)	9916	1824
SPEC A	(English)	9916	43101
Total word count - document A			44925
Total word count - document B			0
Total word count - documents A + B			44925

13/3,AB/23 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00967757
3-PYRIDYL ENANTIOMERS AND THEIR USE AS ANALGESICS
3-PYRIDYLENANTIOMERE UND IHRE VERWENDUNG ALS ANALGETIKA
ENANTIOMERES 3-PYRIDYL ET LEUR UTILISATION COMME ANALGESIQUES
PATENT ASSIGNEE:
Abbott Laboratories, (225075), Chad 0377/AP6D-2, 100 Abbott Park Road, Abbott Park, Illinois 60064-3500, (US), (Proprietor designated states: all)
INVENTOR:
HOLLADAY, Mark, W., 1003 Dawes Street, Libertyville, IL 60048, (US)
ARNERIC, Stephen, P., 1521 Broad Run Rd., Landenberg PA 19350-1330, (US)
BAI, Hao, 327 East Fawn Lane, Grayslake, IL 60030, (US)
DART, Michael, J., 1026 Princeton Avenue, Highland Park, IL 60035, (US)
LIN, Nan-Horng, 432 W Sycamore St., Vernon Hills, IL 60061-1078, (US)
LYNCH, John, K., 8736 44th Avenue, Kenosha, WI 53142, (US)
OR, Yat, Sun, 1107 Wellington Avenue, Libertyville, IL 60048, (US)
RYTHER, Keith, B., 862 Waterview Drive, Round Lake Park, IL 60073, (US)
SULLIVAN, James, P., 705 Dimmydale Drive, Deerfield, IL 60015, (US)
WASICAK, James, T., 28440 Dorie Lane, Waterford, WI 53285, (US)
EHRLICH, Paul, P., 1313 Bull Creek Drive, Libertyville, IL 60048, (US)
LEGAL REPRESENTATIVE:
Modiano, Guido, Dr.-Ing. et al (40786), Modiano, Josif, Pisanty & Staub, Baaderstrasse 3, 80469 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 950057 A1 991020 (Basic)
EP 950057 B1 021113
WO 98025920 980618
APPLICATION (CC, No, Date): EP 97952392 971210; WO 97US22811 971210
PRIORITY (CC, No, Date): US 763278 961210; US 32321 P 961210
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: RO; SI
INTERNATIONAL PATENT CLASS: C07D-401/12; A61K-031/44; C07D-205/04
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200246	2572
CLAIMS B	(German)	200246	2611
CLAIMS B	(French)	200246	2808
SPEC B	(English)	200246	47623
Total word count - document A			0
Total word count - document B			55614
Total word count - documents A + B			55614

13/3,AB/24 (Item 24 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00933023
MEDICINES COMPRISING Rho KINASE INHIBITOR
MEDIKAMENTE ENTHALTEND Rho-KINASE INHIBITOREN
MEDICAMENTS COMPRENANT UN INHIBITEUR DE LA Rho KINASE
PATENT ASSIGNEE:
YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD., (208562), 6-9, Hiranomachi 2-chome Chuo-ku, Osaka-shi Osaka 541, (JP), (Applicant designated States: all)
INVENTOR:
UEHATA, Masayoshi, Yoshitomi Phar. Ind. Ltd., Res. Lab., 7-25, Koyata 3-chome, Iruma-shi, Saitama 358, (JP)
ONO, Takashi, Yoshitomi Pharm. Ind., Ltd, Res. Lab., 7-25, Koyata 3-chome , Iruma-shi, Saitam 358, (JP)
SATOH, Hiroyuki, Yoshitomi Phar. Ind. Ltd., Res. Lab., 955, Oaza-Koiwai, Yoshitomimachi, Chikujo-gun, Fukuoka 871, (JP)
YAMAGAMI, Keiji, Yoshitomi Phar. Ind. Ltd., Res. Lab., 7-25, Koyata 3-chome, Iruma-shi, Saitama 358, (JP)
KAWAHARA, Toshio, Yoshitomi Phar. Ind. Ltd., Res. Lab., 955, Oaza-Koiwai, Yoshitomimachi, Chikujo-gun, Fukuoka 871, (JP)
LEGAL REPRESENTATIVE:
Weber, Thomas, Dr.Dipl.-Chem. et al (75092), Patentanwalte von Kreisler-Selting-Werner, Postfach 10 22 41, 50462 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 956865 A1 991117 (Basic)
WO 9806433 980219
APPLICATION (CC, No, Date): EP 97934756 970808; WO 97JP2793 970808
PRIORITY (CC, No, Date): JP 96212409 960812
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; RO; SI
INTERNATIONAL PATENT CLASS: A61K-045/00; A61K-031/16; A61K-031/165; A61K-031/195; A61K-049/00; A61K-031/445; A61K-031/50; A61K-031/495; A61K-031/44; C07D-213/81; C07D-401/12

ABSTRACT EP 956865 A1
A Rho kinase inhibitor is provided as a novel pharmaceutical agent, particularly as a therapeutic agent of hypertension, a therapeutic agent of angina pectoris, a suppressive agent of cerebrovascular contraction, a therapeutic agent of asthma, a therapeutic agent of peripheral circulation disorder, a prophylactic agent of immature birth, a therapeutic agent of arteriosclerosis, an anti-cancer drug, an anti-inflammatory agent, an immunosuppressant, a therapeutic agent of autoimmune disease, an anti-AIDS drug, a contraceptive, a prophylactic agent of digestive tract infection, a therapeutic agent of osteoporosis, a therapeutic agent of retinopathy and a brain function improving drug. In addition, the Rho kinase inhibitor is provided as a reagent and a diagnostic.
ABSTRACT WORD COUNT: 110

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9946	1777
SPEC A	(English)	9946	13010
Total word count - document A			14787
Total word count - document B			0
Total word count - documents A + B			14787

13/3,AB/25 (Item 25 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00748301
ANTI-INFLAMMATORY COMPOUNDS
ANTIINFLAMMATORISCHE VERBINDUNGEN
COMPOSES ANTI-INFLAMMATOIRES
PATENT ASSIGNEE:
SMITHKLINE BEECHAM CORPORATION, (201246), One Franklin Plaza, Philadelphia, PA 19102, (US), (Proprietor designated states: all)
INVENTOR:
ADAMS, Jerry Leroy, 611 Forest Road, Wayne, PA 19087, (US)
HALL, Ralph Floyd, 1311 Prospect Hill Road, Villanova, PA 19085, (US)
LEE, Dennis, Apartment 502 700 Ardmore Road, Ardmore, PA 19003, (US)
MAYER, Ruth Judik, 115 Reveille Road, Wayne, PA 19087, (US)
SEIBEL, George Leslie, 11 Cornwall Circle, Wayne, PA 19087, (US)
LEGAL REPRESENTATIVE:
Connell, Anthony Christopher et al (69941), SmithKline Beecham plc Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP, (GB)
PATENT (CC, No, Kind, Date): EP 799198 A1 971008 (Basic)
EP 799198 A1 971015
EP 799198 B1 000830
WO 9533461 951214
APPLICATION (CC, No, Date): EP 95922184 950602; WO 95US7010 950602
PRIORITY (CC, No, Date): US 252717 940602
DESIGNATED STATES: BE; CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: C07C-311/21; A61K-031/195; C07C-311/13
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200035	437
CLAIMS B	(German)	200035	394
CLAIMS B	(French)	200035	519
SPEC B	(English)	200035	13765
Total word count - document A			0
Total word count - document B			15115
Total word count - documents A + B			15115

13/3,AB/26 (Item 26 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00746719
ANTI-INFLAMMATORY COMPOUNDS
ENTZUNDUNGSHEMMENDE VERBINDUNGEN
COMPOSES ANTI-INFLAMMATOIRES
PATENT ASSIGNEE:
SMITHKLINE BEECHAM CORPORATION, (201245), UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939, (US), (Proprietor designated states: all)
THE JOHNS HOPKINS UNIVERSITY, (348140), 720 Rutland Avenue, Baltimore, MD 21205, (US), (Proprietor designated states: all)
INVENTOR:

DIXON, James, Scott, SmithKline Beecham, Pharmaceu, ticals R & D, 709 Swedeland Road, King of Prussia, PA 19406, (US)
HALL, Ralph, Floyd, SmithKline Beecham, Pharmaceut, icals R & D, 709 Swedeland Road, King of Prussia, PA 19506, (US)
MARSHALL, Lisa, Ann, SmithKline Beecham, Pharmaceu, ticals R & D, 709 Swedeland Road, King of Prussia, PA 19406, (US)
CHILTON, Floyd, H., Wake Forest University, Medical Center Blvd., Winston Salem, NC 27267-1023, (US)
MAYER, Ruth, Judik, SmithKline Beecham Pharmaceuti, cals R & D, 709 Swedeland Road, King of Prussia, PA 19406, (US)
WINKLER, James, David, SmithKline Beecham Pharmace, uticals R & D, 709 Swedeland Road, King of Prussia, PA 19406, (US)
LEGAL REPRESENTATIVE:
Connell, Anthony Christopher et al (69941), SmithKline Beecham plc Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP, (GB)
PATENT (CC, No, Kind, Date): EP 765305 A1 970402 (Basic)
EP 765305 A1 970903
EP 765305 B1 991215
WO 9533712 951214
APPLICATION (CC, No, Date): EP 95922898 950602; WO 95US6677 950602
PRIORITY (CC, No, Date): US 252716 940602
DESIGNATED STATES: BE; CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: C07C-301/02; A61K-031/21
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9950	623
CLAIMS B	(German)	9950	617
CLAIMS B	(French)	9950	777
SPEC B	(English)	9950	11322
Total word count - document A			0
Total word count - document B			13339
Total word count - documents A + B			13339

13/3,AB/27 (Item 27 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00702636
Protein having TPO activity.
Protein mit TPO-Aktivitat.
Proteine a activite TPO.
PATENT ASSIGNEE:
Kirin Brewery Company, Ltd., (789432), 10-1, 2-chome, Shinkawa, Chuo-ku, Tokyo, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Miyazaki, Hiroshi, 817-17 Shimonojo-machi Takasaki-shi, Gunma-ken, (JP)
Kato, Takashi, 819-8 Shimonojo-machi Takasaki-shi, Gunma-ken, (JP)
Ohgami, Kinya, B-102 Shikishima-Ryo 2-37-16 Kami-Koide-machi, Maebashi-shi Gunma-ken, (JP)
Iwamatsu, Akihiro, Belvedere A201 6-20-42 Tomiokahigashi, Kanazawa-ku Yokohama-shi Kanagawa-ken, (JP)
Akahori, Hiromichi, 3439-78-2 Ishihara-machi Takasaki-shi, Gunma-ken, (JP)

Kuroki, Ryota, 13-20-2, Noukendai 5-chome Kanazawa-ku, Yokohama.shi, (JP)
Shimizu, Toshiyuki, 35-6-101, Noukendai 6-chome Kanazawa-ku, Yokohama-shi Kanagawa-ken, (JP)
Muto, Takanori, Kanazawahakkei-Ryo 102 2-8-4 Teramae, Kanazawa-ku Yokohama-shi Kanagawa-ken, (JP)
LEGAL REPRESENTATIVE:
UEXKULL & STOLBERG Patentanwalte (100011), Beselerstrasse 4, D-22607 Hamburg, (DE)
PATENT (CC, No, Kind, Date): EP 668352 A1 950823 (Basic)
APPLICATION (CC, No, Date): EP 95200385 950214;
PRIORITY (CC, No, Date): JP 9439090 940214; JP 9479842 940325; JP 94155126 940601; JP 94167328 940615; JP 94227159 940817; JP 94304167 941101; JP 94341200 941228; JP 94193169 940817; JP 94298669 941201; JP 94193916 940818; US 212164 940314; US 221020 940401; US 278083 940720; US 320300 941011; US 361811 941222; US 381478 950131
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/19

ABSTRACT EP 668352 A1
The present invention relates to thrombopoietin (TPO) polypeptides having the biological activity of specifically stimulating or increasing platelet production comprising the amino acid sequence 1-332 of SEQ ID NO: 6 or a derivative thereof, DNA molecules encoding TPO polypeptides, processes for production of the polypeptides, antibodies specifically immunoreactive with the polypeptides, pharmaceutical compositions comprising the polypeptides, and methods for using the polypeptides in treatment of platelet disorders such as thrombocytopenia. (see image in original document)
ABSTRACT WORD COUNT: 77

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	1234
SPEC A	(English)	EPAB95	73519
Total word count - document A			74753
Total word count - document B			0
Total word count - documents A + B			74753

13/3,AB/28 (Item 28 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00637707
MONOCLONAL ANTIBODIES DIRECTED AGAINST THE MICROTUBULE-ASSOCIATED PROTEIN TAU, HYBRIDOMAS SECRETING THESE ANTIBODIES, ANTIGEN RECOGNITION BY THESE MONOCLONAL AN
MONOKLONALE ANTIKORPER GEGEN DAS MIKROTUBULUSASSOZIIERTE TAUPROTEIN,HYBRIDOMEN, DIE DIESE ANTIKORPER SEZERNIEREN, ANTIGENERKENNUNG DURCH DIESE MONOKLONALEN ANTI
ANTICORPS MONOCLONAUX DIRIGES CONTRE LA PROTEINE TAU ASSOCIEE AUX MICROTUBULES, HYBRIDOMES SECRETANT CES ANTICORPS, RECONNAISSANCE D'ANTIGENES PAR CES ANTICORPS
PATENT ASSIGNEE:
N.V. INNOGENETICS S.A., (713141), Industriepark Zwijnaarde 7, Box 4, 9052 Gent, (BE), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)

INVENTOR:
VANDERMEEREN, Marc, Armand Preud'Homme Straat 10, B-2440 Geel, (BE)
MERCKEN, Marc, Durhamstreet 5A, Somerville, MA 02143, (US)
VANMECHELEN, Eugeen, Ten Edestraat 101, B-9810 Nazareth-Eke, (BE)
VAN DE VOORDE, Andre, Groenstraat 22, B-9160 Lokeren, (BE)
LEGAL REPRESENTATIVE:
De Clercq, Ann G. Y. (87751), Innogenetics N.V., Industriepark Zwijnaarde 7, P.O. Box 4, 9052 Gent, (BE)
PATENT (CC, No, Kind, Date): EP 673418 A1 950927 (Basic)
EP 673418 B1 980506
WO 9413795 940623
APPLICATION (CC, No, Date): EP 94903752 931210; WO 93EP3499 931210
PRIORITY (CC, No, Date): EP 92403403 921214
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/06; C12P-021/08; C12N-005/20; C07K-016/18; C07K-014/47; G01N-033/577; G01N-033/68;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9819	1242
CLAIMS B	(German)	9819	1225
CLAIMS B	(French)	9819	1342
SPEC B	(English)	9819	8015
Total word count - document A			0
Total word count - document B			11824
Total word count - documents A + B			11824

13/3,AB/29 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00625833
MONOCLONAL ANTIBODIES DIRECTED AGAINST THE MICROTUBULE-ASSOCIATED PROTEIN TAU
Monoklonale Antikorper gegen das mikrotubulusassoziierte Protein Tau.
ANTICORPS MONOCLONAUX DIRIGES CONTRE LA PROTEINE TAU ASSOCIEE AUX MICROTUBULES
PATENT ASSIGNEE:
N.V. INNOGENETICS S.A., (713141), Industriepark Zwijnaarde 7, Box 4, 9052 Gent, (BE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;SE)
INVENTOR:
MERCKEN, Marc, 5A Durhamstreet, Somerville, MA 02143, (US)
MANDELKOW, Eva-Maria, Baron-Voght-Strasse 212a, D-2000 Hamburg 52, (DE)
VANDERMEEREN, Marc, Armand Preud'Homme Straat 10, B-2440 Geel, (BE)
VANMECHELEN, Eugeen, Ten Edestraat 101, B-9810 Nazareth-Eke, (BE)
VAN DE VOORDE, Andre, Groenstraat 22, B-9160 Lokeren, (BE)
LEGAL REPRESENTATIVE:
Gutmann, Ernest et al (15992), Ernest Gutmann - Yves Plasseraud S.A. 3, rue Chauveau-Lagarde, F-75008 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 610330 A1 940817 (Basic)
EP 610330 B1 970618
WO 9308302 930429
APPLICATION (CC, No, Date): EP 92922432 921017; WO 92EP2392 921017
PRIORITY (CC, No, Date): EP 91402871 911025

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/08; C12N-005/20; C07K-002/00; C12N-015/06; G01N-033/577;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB97	1415
CLAIMS B	(German)	EPAB97	1414
CLAIMS B	(French)	EPAB97	1490
SPEC B	(English)	EPAB97	8084
Total word count - document A			0
Total word count - document B			12403
Total word count - documents A + B			12403

13/3,AB/30 (Item 30 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00612002
IMMUNOTOXINS DIRECTED AGAINST c-erbB-2 (HER-2/neu) RELATED SURFACE ANTIGENS
GEGEN C-ERB B-2 (HER-2/NEU) VEWANDTE OBERFLACHENANTIGENE GERICHTETE IMMUNTOXINE
IMMUNOTOXINES DIRIGEES CONTRE DES ANTIGENES DE SURFACE APPARENTEES A c-erbB-2 (HER-2/neu)
PATENT ASSIGNEE:
RESEARCH DEVELOPMENT FOUNDATION, (1119572), 402 North Division Street, Carson City, Nevada 89703, (US), (Proprietor designated states: all)
INVENTOR:
ROSENBLUM, Michael G., 8810 North Rylander Circle, Houston, TX 77071, (US)
SHAWVER, Laura K., 216 Cotter street, San Fransisco, CA 94112-1933, (US)
LEGAL REPRESENTATIVE:
Wilkinson, Stephen John et al (52061), Stevens, Hewlett & Perkins 1 St. Augustine's Place, Bristol BS1 4UD, (GB)
PATENT (CC, No, Kind, Date): EP 635030 A1 950125 (Basic)
EP 635030 A1 980708
EP 635030 B1 040721
WO 1993021232 931028
APPLICATION (CC, No, Date): EP 93912147 930408; WO 93US3292 930408
PRIORITY (CC, No, Date): US 867728 920410
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-014/415; A61K-039/395; A61K-047/48
NOTE:
No A-document published by EPO
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200430	564
CLAIMS B	(German)	200430	552
CLAIMS B	(French)	200430	599
SPEC B	(English)	200430	10676
Total word count - document A			0
Total word count - document B			12391

Total word count - documents A + B 12391

13/3,AB/31 (Item 31 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00601361
Pharmaceutical compositions containing **botulinum toxin** and method of preparation.
Pharmazeutische Zusammensetzungen, die Botulinumtoxin enthalten und Verfahren zur Herstellung.
Compositions pharmaceutiques contenant la **toxine** de **botulinum** et procede de preparation.
PATENT ASSIGNEE:
WISCONSIN ALUMNI RESEARCH FOUNDATION, (319666), P.O. Box 7365, Madison, WI 53705-7365, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Schantz, Edward J., 5102 South Hill Drive, Madison WI 53705, (US)
Goodnough, Michael C., 6914 Harvest Hill Road, Madison WI 53717, (US)
Johnson, Eric A., 3901 Council Court, Madison WI 53711, (US)
LEGAL REPRESENTATIVE:
Ellis-Jones, Patrick George Armine (30442), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 593176 A2 940420 (Basic)
EP 593176 A3 950301
APPLICATION (CC, No, Date): EP 93307656 930928;
PRIORITY (CC, No, Date): US 951604 920928
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/08;

ABSTRACT EP 593176 A2
A pharmaceutical composition contains active lyophilized **botulinum toxin** type **A**, no **sodium chloride** and less than about 25 % inactive toxin is disclosed along with a method of preparing it.
ABSTRACT WORD COUNT: 32

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	190
SPEC A	(English)	EPABF2	1928
Total word count - document A			2118
Total word count - document B			0
Total word count - documents A + B			2118

13/3,AB/32 (Item 32 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00577652
COMPOSITIONS AND METHODS FOR IDENTIFYING BIOLOGICALLY ACTIVE MOLECULES
ZUSAMMENSETZUNGEN UND VERFAHREN ZUR IDENTIFIZIERUNG VON MOLEKULEN MIT BIOLOGISCHER WIRKSAMKEIT
COMPOSITIONS ET PROCEDES D'IDENTIFICATION DE MOLECULES BIOLOGIQUEMENT

ACTIVES
PATENT ASSIGNEE:
CHIRON CORPORATION, (572535), 4560 Horton Street, Emeryville, California 94608-2916, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
DEVLIN, James, J., 1146 Upper Happy Valley, Lafayette, CA 94549, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 600866 A1 940615 (Basic)
EP 600866 B1 971203
WO 9118980 911212
APPLICATION (CC, No, Date): EP 91910915 910513; WO 91US3332 910513
PRIORITY (CC, No, Date): US 533180 900601
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/10; C12N-015/62; C12N-015/34; C12N-015/70; C12N-015/00; C07K-007/06
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9711W4	302
CLAIMS B	(German)	9711W4	239
CLAIMS B	(French)	9711W4	350
SPEC B	(English)	9711W4	7112
Total word count - document A			0
Total word count - document B			8003
Total word count - documents A + B			8003

13/3,AB/33 (Item 33 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00558043
GENETICALLY ENGINEERED VACCINE STRAIN
GENTECHNOLOGISCH HERGESTELLTER STAMM FUR IMPFSTOFFE
SOUCHE DE VACCIN MISE AU POINT PAR GENIE GENETIQUE
PATENT ASSIGNEE:
VIROGENETICS CORPORATION, (1534420), 465 Jordan Road, Rensselaer Technology Park, Troy, NY 12180, (US), (Proprietor designated states: all)
INVENTOR:
PAOLETTI, Enzo, 297 Murray Avenue, Delmar, NY 12054, (US)
PERKUS, Marion E., Box 267A, R.D. No. 2, 4971 Western Turnpike, Altamont, NY 12009, (US)
TAYLOR, Jill, 33 Colonial Avenue, Albany, NY 12203, (US)
TARTAGLIA, James, 7 Christina Drive, Schenectady, NY 12303, (US)
NORTON, Elizabeth, K., 33 Cayuga Court, Averill Park, New York 12018-9672, (US)
RIVIERE, Michel, 11, chemin du Chancellier, F-69130 Ecully, (FR)
DE TAISNE, Charles, 48 bis, rue du Commandant-Charcot, F-69005 Lyon, (FR)
LIMBACH, Keith, J., 324 Hampton Place, Troy, NY 12180, (US)
JOHNSON, Gerard, P., 100 Devitt Road, Waterford, NY 12188, (US)
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GETTIG, Russell, Robert, R.D. 2, Box 421C, Averill Park, NY 12018, (US)
LEGAL REPRESENTATIVE:
Harding, Charles Thomas et al (70742), D. Young & Co. 21 New Fetter Lane, London EC4A 1DA, (GB)
PATENT (CC, No, Kind, Date): EP 575491 A1 931229 (Basic)
EP 575491 A1 941012
EP 575491 B1 030813
WO 92015672 920917
APPLICATION (CC, No, Date): EP 92908110 920309; WO 92US1906 920309
PRIORITY (CC, No, Date): US 666056 910307; US 713967 910611; US 847951 920306
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003018214)
INTERNATIONAL PATENT CLASS: C12N-007/00; A61K-039/12; C12N-015/863
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200333	453
CLAIMS B	(German)	200333	389
CLAIMS B	(French)	200333	595
SPEC B	(English)	200333	100952
Total word count - document A			0
Total word count - document B			102389
Total word count - documents A + B			102389

13/3,AB/34 (Item 34 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00499265
A NEW METHOD FOR DETECTING A SPECIFIC NUCLEIC ACID SEQUENCE IN A SAMPLE OF CELLS
NEUES VERFAHREN ZUM NACHWEIS EINER SPEZIFISCHEN NUKLEINSAURESEQUENZ IN EINER ZELLPROBE
NOUVELLE METHODE PERMETTANT DE DETECTER UNE SEQUENCE D'ACIDE NUCLEIQUE SPECIFIQUE A PARTIR D'UN PRELEVEMENT DE CELLULES
PATENT ASSIGNEE:
Pharmacia Biotech AB, (1345733), , 751 82 Uppsala, (SE), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
FROSTELL, Asa, Norrtaljeg 7A, S-75327 Uppsala, (SE)
NUNN, Michael, F., 699 South Nardo Avenue, T6, Solana Beach, CA 92075, (US)
LEGAL REPRESENTATIVE:
Widen, Bjorn et al (39502), Pharmacia & Upjohn AB, Patent Department, 751 82 Uppsala, (SE)
PATENT (CC, No, Kind, Date): EP 504278 A1 920923 (Basic)
EP 504278 A1 930609
EP 504278 B1 970115
WO 9108308 910613
APPLICATION (CC, No, Date): EP 91901361 901129; WO 90US6953 901129
PRIORITY (CC, No, Date): US 443910 891130; US 505833 900406; US 548027 900705

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12Q-001/68; C12Q-001/70; C12N-015/11;
C12N-005/10;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB97	798
CLAIMS B	(German)	EPAB97	703
CLAIMS B	(French)	EPAB97	879
SPEC B	(English)	EPAB97	11640

Total word count - document A 0
Total word count - document B 14020
Total word count - documents A + B 14020

13/3,AB/35 (Item 35 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00498736
ANTIVENOMS AND METHODS FOR MAKING ANTIVENOMS
GEGENGIFTE UND VERFAHREN ZU DEREN HERSTELLUNG
SERUMS ANTIVENIMEUX ET LEURS PROCEDES DE FABRICATION
PATENT ASSIGNEE:
CARROLL, Sean B., (1373820), 3066 Streb Way, Cottage Grove, WI 53527, (US), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
CARROLL, Sean B., 3066 Streb Way, Cottage Grove, WI 53527, (US)
LEGAL REPRESENTATIVE:
Glawe, Delfs, Moll & Partner (100692), Patentanwalte Postfach 26 01 62, 80058 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 498854 A1 920819 (Basic)
EP 498854 A1 930303
EP 498854 B1 980826
WO 9106306 910516
APPLICATION (CC, No, Date): EP 91900530 901031; WO 90US6341 901031
PRIORITY (CC, No, Date): US 429791 891031
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-035/16; A61K-039/395; C07K-001/00; C07K-017/08; C07K-002/00; G01N-033/538; C08G-063/48;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9835	3496
CLAIMS B	(German)	9835	3591
CLAIMS B	(French)	9835	3977
SPEC B	(English)	9835	31700

Total word count - document A 0
Total word count - document B 42764
Total word count - documents A + B 42764

13/3,AB/36 (Item 36 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00459428
Human monoclonal antibodies against bacterial toxins.
Menschliche monoklonale Antikorper gegen bakterielle Toxine.
Anticorps monoclonaux humains contre des toxines bacteriennes.
PATENT ASSIGNEE:
THE UNIVERSITY OF ROCHESTER, (290260), 601 Elmwood Avenue, Rochester, New York 14642, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Insel, Richard Alan, 167 Oakdale Drive,, Rochester, New York 14618, (US)
Gigliotti, Francis, 63 Caversham Woods, Pittsford, New York 14534, (US)
LEGAL REPRESENTATIVE:
Warcoin, Jacques et al (19071), Cabinet Regimbeau 26, avenue Kleber, F-75116 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 440266 A2 910807 (Basic)
EP 440266 A3 910828
APPLICATION (CC, No, Date): EP 91105163 830929;
PRIORITY (CC, No, Date): US 428747 820930
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 105804
INTERNATIONAL PATENT CLASS: C12N-015/08; C12N-005/28; C12P-021/08; A61K-039/40;

ABSTRACT EP 440266 A2
The production of stable hybrid cell lines that secrete human monoclonal antibodies against bacterial toxins by fusing post-immunization human peripheral blood lymphocytes with nonsecretor mouse myeloma cells is described. Using the method, protective monoclonal antibodies against tetanus toxin and diphtheria toxin were produced that bind tetanus toxin and diphtheria toxin in vitro, respectively, and prevent tetanus and diphtheria in vivo in animals, respectively.
ABSTRACT WORD COUNT: 65

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1133
SPEC A	(English)	EPABF1	10206
Total word count - document A			11339
Total word count - document B			0
Total word count - documents A + B			11339

13/3,AB/37 (Item 37 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00338241
Chemically regulatable DNA sequences and genes and uses thereof.
Chemisch regulierte Sequenzen und Gene, und ihre Verwendungen.
Sequences d'ADN et genes chimiquement regulables, et leur emploi.
PATENT ASSIGNEE:
CIBA-GEIGY AG, (201300), Klybeckstrasse 141, CH-4002 Basel, (CH), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Ryals, John, 415 Dunhill Circle, Durham, NC 27713, (US)

Montoya, Alice, , deceased, (US)
Harms, Christian, 1412 Gray Bluff Trail, Chapel Hill, NC 27514, (US)
Duesing, John, Gatternweg 18, CH-4125 Riehen, (CH)
Sperisen, Christoph, Landskronstrasse 4, CH-4056 Basel, (CH)
Meins, Fred, Leimgrubenweg 52, CH-4125 Riehen, (CH)
Payne, George, 804 B7 Park Ridge Road, Durham, NC 27713, (US)
LEGAL REPRESENTATIVE:
Zumstein, Fritz, Dr. et al (13567), Patentanwalte, Dr. F. Zumstein, Dipl.-Ing. F. Klingseisen, Brauhausstrasse 4, 80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 332104 A2 890913 (Basic)
EP 332104 A3 910320
APPLICATION (CC, No, Date): EP 89103888 890306;
PRIORITY (CC, No, Date): US 165667 880308; US 305566 890206
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00;

ABSTRACT EP 332104 A2
The present invention provides chemically regulatable DNA sequences capable of regulating transcription of an associated DNA sequence in plants or plant tissues, chimeric constructions containing such sequences, vectors containing such sequences and chimeric constructions, and transgenic plants and plant tissues containing these chimeric constructions. Also provided are a novel signal peptide sequence, genes which code for this sequence, and newly identified PR protein genes. The chimeric constructions and transgenic plants and plant tissues may be used in an assay for new chemical regulators.
ABSTRACT WORD COUNT: 87

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	3526
SPEC A	(English)	EPABF1	33592
Total word count - document A			37118
Total word count - document B			0
Total word count - documents A + B			37118

13/3,AB/38 (Item 38 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00273288
Pharmaceutically active compounds.
Pharmazeutische aktive Verbindungen.
Composes pharmaceutiques actifs.
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Girijavallabhan, Viyyoor Moopil, 10 Maplewood Drive, Parsippany, N.J. 07054, (US)
Pinto, Patrick Anthony, 232 Randolph Avenue, Mine Hill, N.J. 07801, (US)
Ganguly, Ashit Kumar, 96 Cooper Avenue, Upper Montclain, N.J. 07043, (US)
Versace, Richard William, 65B Townsend Road, Wanaque, N.J. 07465, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)

PATENT (CC, No, Kind, Date): EP 274867 A2 880720 (Basic)
EP 274867 A3 901114
EP 274867 B1 940413
APPLICATION (CC, No, Date): EP 87310807 871209;
PRIORITY (CC, No, Date): US 940125 861210
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07D-233/60; A61K-031/415; C07D-277/36; C07D-257/04; C07D-213/70; C07D-257/06; C07D-213/30; C07D-239/54; C07D-233/70; C07D-233/94; C07D-235/06;

ABSTRACT EP 274867 A2

The disclosed invention is compounds represented by the formula (see image in original document) and pharmaceutically acceptable acid addition, basic addition and quarternary amine salts thereof and pharmaceutically acceptable solvates thereof, wherein

each Z is independently tetiary butyl, phenyl, naphthyl or adamantyl; substituted phenyl, wherein the substituents are one or more of halogen, lower alkoxy, phenoxy, nitrile, nitro, phenyslsulfonyl, loweralkylsulfonyl, oxazol-2-yl, lower alkanoyl, benzoyl, lower alkoxycarbonyl, lower alkyl, lower alkylthio, phenyl, phenylaminothiocarbonyl, or lower alkylaminothiocarbonyl; 4 or 6 membered unsubstituted or substituted heterocyclic ring containing at least one nitrogen with the remaining members of the ring being at least one carbon, and optionally sulfur or oxygen, wherein the substituents are one or more of carboxyl, hydroxymethyl, lower alkyl, loweralkylcarbonyl or aryl lower alkyl;

X and Y are each independently a bond, -O-, (see image in original document) each Q is independently a divalent substituted or unsubstituted, straigh or branched chain lower alkanediyl, lower alkanediyl-cycloalkaneidyl-lower alkanediyl, lower alkenediyl, lower alkynediyl, phenylene, dihydrofurandiyl, tetrahydrofurandiyl, tetrahydropyrandiyl, or, loweralkanediyl-tetrahydrofurandiyl-loweralkanediyl, wherein the substituents are one or more of hydroxy, epoxy, fluorine, chlorine, azide, or amino;

W is a monovalent substituted or unsubstituted aryl group or a heterocyclic single or fused ring containing from 4 to 10 ring atoms, at least one hetero atom of which is a nitrogen atom and the remaining ring atoms being at least one carbon and optionally sulfur or oxygen, wherein the substituents are one or more of hydroxy, oxo amino, carbamoyl, carboxyl, nitrile, nitro, lower alkoxy carbonyl, halogen, sulfamyl, lower alkyl, lower alkylthio, lower alkoxy, hydroxyloweralkyl, lower alkoxycarbonylloweralkyl, amino loweralkyl, carboxyloweralkyl, guanidino, thioureido, lower alkylsulfonylamino, aminocarbonylloweralkyl, allyloxycarbonylmethyl or carbamoyloxyloweralkyl; with the proviso that W cannot be substituted or unsubstituted isoxazolyl, and

W(') is divalent W.

The compounds have antiviral activity, antiinflammatory activity and are PAF inhibitors.

ABSTRACT WORD COUNT: 303

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	2124
CLAIMS B	(German)	EPBBF1	1950
CLAIMS B	(French)	EPBBF1	2249
SPEC B	(English)	EPBBF1	6876

Total word count - document A 0

Searcher : Shears 571-272-2528

Total word count - document B 13199
Total word count - documents A + B 13199

13/3,AB/39 (Item 39 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00113752
Human monoclonal antibodies against bacterial toxins.
Menschliche monoklonale Antikorper gegen bakterielle Toxine.
Anticorps monoclonaux humains contre des toxines bacteriennes.
PATENT ASSIGNEE:
THE UNIVERSITY OF ROCHESTER, (290260), 601 Elmwood Avenue, Rochester, New York 14642, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Insel, Richard Alan, 167 Oakdale Drive, Rochester New York 14618, (US)
Gigliotti, Francis, 25 N. Alicia Drive, Memphis Tennessee 38112, (US)
LEGAL REPRESENTATIVE:
Martin, Jean-Jacques et al (17181), Cabinet REGIMBEAU 26, Avenue Kleber, F-75116 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 105804 A2 840418 (Basic)
EP 105804 A3 860813
EP 105804 B1 911211
APPLICATION (CC, No, Date): EP 83401913 830929;
PRIORITY (CC, No, Date): US 428747 820930
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/08;

ABSTRACT EP 105804 A2
Human monoclonal antibodies against bacterial toxins.
The production of stable hybrid cell lines that secrete human monoclonal antibodies against bacterial toxins by fusing post-immunization human peripheral blood lymphocytes with nonsecretor mouse myeloma cells is described. Using the method, protective monoclonal antibodies against tetanus toxin and diphtheria toxin were produced that bind tetanus toxin and diphtheria toxin in vitro, respectively, and prevent tetanus and diphtheria in vivo in animals, respectively.
ABSTRACT WORD COUNT: 71

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	162
CLAIMS B	(German)	EPBBF1	167
CLAIMS B	(French)	EPBBF1	178
SPEC B	(English)	EPBBF1	10188

Total word count - document A 0
Total word count - document B 10695
Total word count - documents A + B 10695

Set	Items	Description
S14	173	AU=(MOYER, E? OR MOYER E?)
S15	7	AU=(HIRTZER, P? OR HIRTZER P?)
S16	1	S14 AND S15
S17	14	(S14 OR S15) AND S3
S18	1	S17 AND S2
S19	0	(S16 OR S18) NOT S12

- Author(s)

Searcher : Shears 571-272-2528

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File  65:Inside Conferences 1993-2005/Oct W4
         (c) 2005 BLDSC all rts. reserv.
File 440:Current Contents Search(R) 1990-2005/Oct 27
         (c) 2005 Inst for Sci Info
File 348:EUROPEAN PATENTS 1978-2005/Oct W03
         (c) 2005 European Patent Office
File 357:Derwent Biotech Res. _1982-2005/Oct W5
         (c) 2005 Thomson Derwent & ISI
File 113:European R&D Database 1997
         (c)1997 Reed-Elsevier(UK)Ltd All rts reserv

Set     Items   Description
S1    4607135   (BO OR BOTULIN?)(5N)(NT OR NEUROTOXIN? ? OR TOXIN? ? OR TO-
              X??) OR BOTOX?? OR BONT?? OR BOTX?? OR BTX?? OR (BT OR BN OR -
              BNT??)(10N)BOTULIN? OR BOTULIN?(3A)(A OR B OR C1 OR C2 OR D OR
               E OR F OR G)
S2      10936   (BO OR BOTULIN?)(5N)(NT OR NEUROTOXIN? ? OR TOXIN? ? OR TO-
              X??) OR BOTOX?? OR BONT?? OR BOTX?? OR BTX?? OR (BT OR BN OR -
              BNT??)(10N)BOTULIN? OR BOTULIN?(3N)(A OR B OR C1 OR C2 OR D OR
               E OR F OR G)
S3     517116   PHOSPHATE OR SUCCINATE OR SUCCINIC OR ACETATE OR CITRATE OR
              BUTANEDIOIC OR ACETIC
S4        901   S2 AND S3
S5        335   S4 AND (NACL OR (NA OR SODIUM)(W)(CL OR CHLORIDE) OR SALIN-
              E)
S6        158   S5 AND (HSA(S)ALBUMIN OR SER??(W)ALBUMIN OR GELATIN? ?)
S7        146   S6 AND BUFFER?
S8        131   S7 AND (TEMP? ? OR TEMPERATURE? ?)
S9        125   S8 AND (PH OR (HYDROGEN OR H)(W)ION)
S10         7   S9 AND (CENTIGRADE OR CELSIUS)
S11        33   S9 AND ((UNIT? ? OR U)(2N)(ML OR MILLILIT? OR MILLI(W)(LIT-
              ER? OR LITRE?)))
S12        39   S10 OR S11
S13        39   RD (unique items)
S14       173   AU=(MOYER, E? OR MOYER E?)
S15         7   AU=(HIRTZER, P? OR HIRTZER P?)
S16         1   S14 AND S15
S17        14   (S14 OR S15) AND S3
S18         1   S17 AND S2
S19         0   (S16 OR S18) NOT S12
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